POLYSULPHONYL METHANES.

A CONTRIBUTION TO THE
ORGANIC CHEMISTRY OF
SULPHUR.

THESIS

PRESENTED FOR THE DEGREE OF
DOCTOR OF SCIENCE

by

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CARNEGIE TEACHING FELLOW

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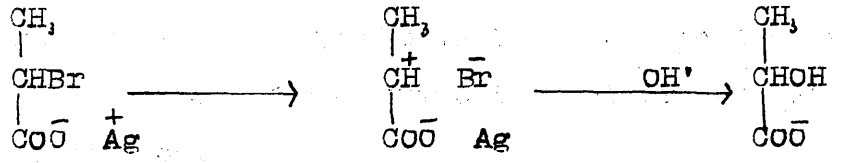
C O N T E N T S.

Frankland, in his Presidential lecture[1] to the Chemical Society, pointed out that 'in the classical investigations of Pope and Peachey[2] and Smiles[3] on the optically active derivatives of Sulphur, Selenium and Tin, the compounds had their rotatory power determined in the ionised state, with the asymmetric atom involved in the ionisation! He went on to say that ' there is abundant evidence that a tetravalent asymmetric atom can retain its activity in the ionised condition ' and he added that 'there is, however, very striking evidence that the asymmetry in such cases is very unstable..... and quite unlike anything encountered in the optically active compounds of Carbon.

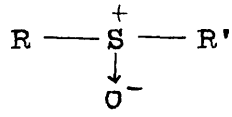
Likewise, Sidgwick,[4] in developing his concept of co-valency maxima, instances many important differences between carbon and other elements which exhibit tetravalency, e.g. the stability of the hydrocarbons contrasted with the reactivity of the silanes. He points out that the characteristic of carbon is its extreme reluctance to abandon the 4 covalent condition, that it only forms an electro-valent linkage as a method of escape from the 3 covalent condition of such compounds as the triphenyl methyls.

From time to time theories of the mechanism of the Walden Inversion have assumed the possibility of a charged carbon atom retaining its asymmetry - at least momentarily - while attached to only three other radicles.

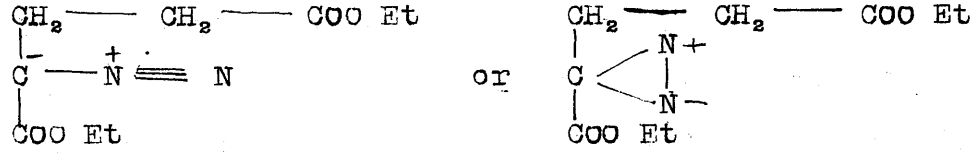


active active

This hypothesis has been strengthened by Philips' resolution of a sulphoxide[5]

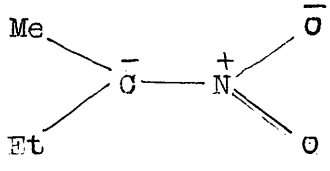


but the only direct evidence is Noyes' preparation of an optically active specimen of ethyl diazoglutarate.[6]



Quite apart from the uncertainty between the formulae, the experimental details reveal that the observed rotations were low, and, in spite of precautions, the chances of impurity were high, as the substance was not obtained crystalline.

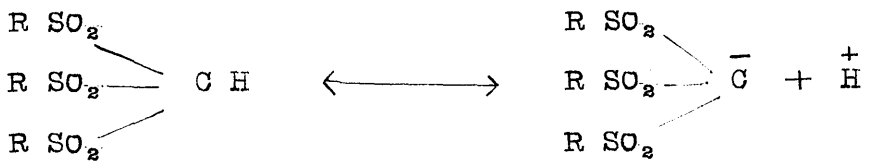
A more definite case is provided by Kuhn, who observed activity in alkaline solutions of secondary nitrobutane.[7]



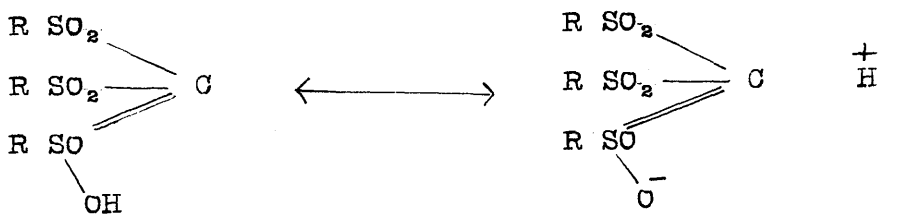
As the activity can scarcely be attributed to oxygen or to nitrogen, Kuhn contended that it is due to the negatively charged carbon atom.

It seemed therefore, well worth attempting the isolation of a compound whose activity should be unequivocally dependent on a carbon atom attached to four different groups, one of them by an electrovalency.

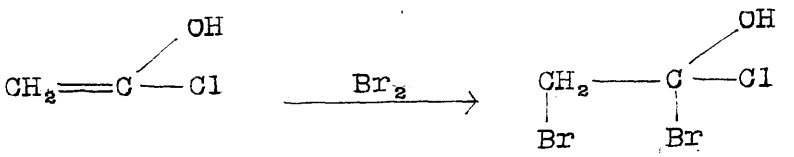
A review of the literature[8] revealed that the polysulphonyl methanes are relatively strong acids and suggested them a suitable type to test the hypothesis of an optically active carbon ion.



It may be objected that since the CH group is activated by sulphone radicles some tautomerism analogous to the enolisation of the $CH_2.CO$ group might lead to the production of an ion which could not be asymmetric :-



Actually, a suggestion of enolisation has been put forward by Aschan[9]. He shewed that acetyl chloride reacts with bromide:



and this lead him to suggest that sulphonyl chlorides might react similarly

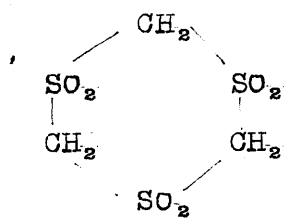
He does not appear to have tried the experiment, or to have been aware that McGowan attempted it many years earlier with no success.[10] In the absence, therefore, of any direct evidence for enolisation, the trisulphonyl methanes seemed a suitable class in which to seek a test case of the active carbon ion.

When the investigation was actually under way, Shriner[11] made the claim* that the solubility of bis-phenyl sulphonyl methane in alkali constituted "the first case in which the position of the residual charge charge is unquestionably on the methylene carbon atom" for "it is obviously impossible to write any other formula without violating the principles of the octet theory"

$$\left[Ph\ SO_2\ \overset{-}{C}H\ SO_2\ Ph\right]\quad \overset{+}{Na}$$

He says that the salt is not formed by the ionisation of the enol form"

The most readily accessible sulphonyl methanes are derived from trimethylene trisulphone :-



but preliminary experiment soon showed that they were too insoluble, were too infusible, and offered quite exceptional difficulties in analysis. These difficulties disappear in the Dithiolan series, and so experiments were undertaken to synthesise the related trisulphone :-

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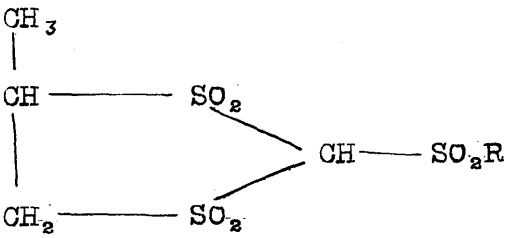
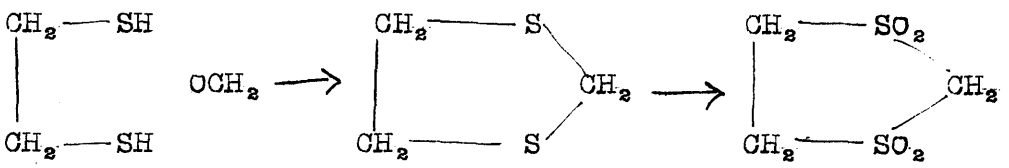
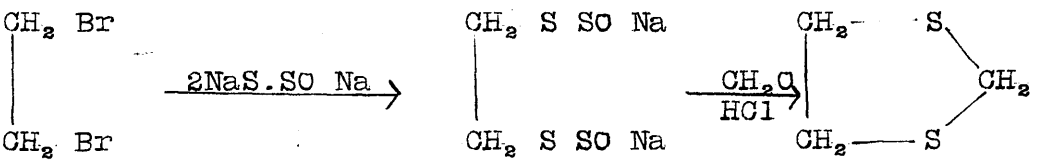
* Potassium derivatives of trimethylene trisulphone were isolated by Camps[12] in 1890 and many similar derivatives known to Trögen 1900-1920.
The 'position of the residual charge' is not stated in so many words, but rather implied by formulae by them.



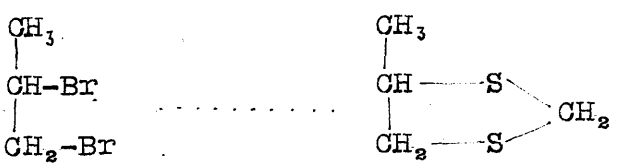
Baumann and Walter obtained Dithiolan disulphone from ethylene mercaptan[13] :-



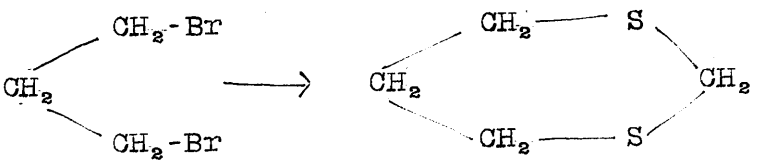
but when their work was repeated, the odours were so disgusting that a new process was devised.



It was most unexpected that 1,2 dibromo propane was absolutely unaffected by this treatment.

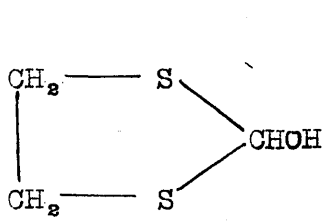


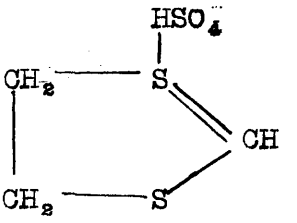
the more especially as 1,3 dibromo propane reacted quite smoothly:



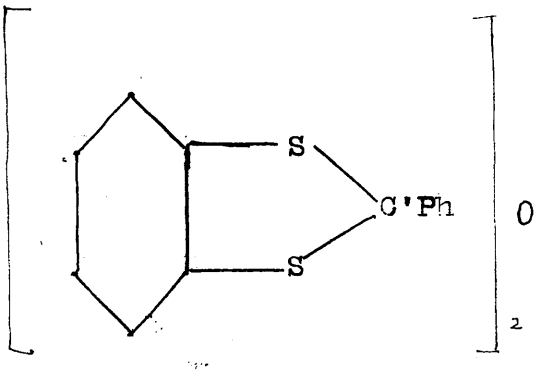
When cleaning the apparatus used in some of these experiments, remarkably beautiful and characteristic colours were

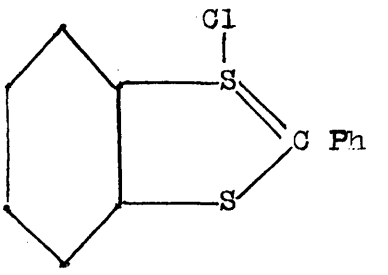
observed with acid solvents. It was eventually found that dithiolan can give rise to an intermediate monoxide :-





Its coloured solutions in acid media are probably due to psuedo-basicity, just as with benzdithiolene oxide.[14]

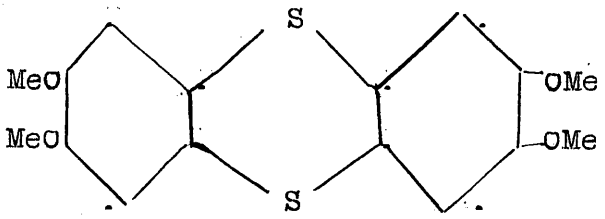




Moreover, the monoxide gives a complex chloroplatinate analogous to that obtained by Tschugaev[15] from dimethyl sulphide

$$\left[(CH_3S)_4\ Pt\right]\ PtCl_6 \qquad \left[\left(C_3H_5S)_2O\right)_2\ Pt\right]\ PtCl_6$$

Again, under the action of hydrochloric acid, one molecule of the monoxide is readily oxidised at the expense of another, so that one half of the material is recovered as Dithiolan, the other as an insoluble dioxide. Shortly after this was noted, a rather similar observation was made by Fries[16] working on Tetramethoxy-thianthrene :

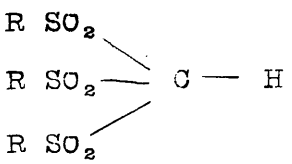


He found that it dissolved with the evolution of sulphur dioxide in concentrated sulphuric acid to give a blue solution. This oxidation product underwent hydrolysis to give equal parts of the Thianthrene and its Monoxide.

COLOURS WITH CONCENTRATED SULPHURIC ACID.

Dithiolan (crude)	Cold	Red
	warm + anisole	Purple → Brown.
Dithiolan (pure)	warm	Pale red
	+ anisole	Yellow → Green →
		→ Blue → Brown.
Dithiolan monoxide	Cold	Green → Red
	+ anisole	Red → Purple → Brown.

In spite of the improved methods, the Dithiolans were persistently obnoxious, and so the open chain sulphones were examined .



The existing data indicated that they would be more soluble and fusible and obtainable without odour. The methods, by which they had been obtained,[8] did not, however, lend themselves to the economical preparation of sulphonyl methanes in which the substituents R are all different.

Accordingly, the possibility of extending Smiles' reaction[17]

$$R\,CO\,CH_2\,CO\,R \xrightarrow{Ph\,SO_2\,S\,Ph} R\,CO\,\underset{\displaystyle S\,Ph}{\underset{|}{CH}}\,CO\,R$$

was explored.

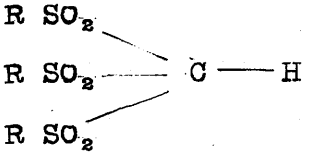
THE TRISULPHONYL METHANES.

The preparation of trisulphonyl methanes falls into two sections.

(1) The preparation of a disulphonyl-methane.

$$R\ SO_2\ CH_2\ SO_2\ R$$

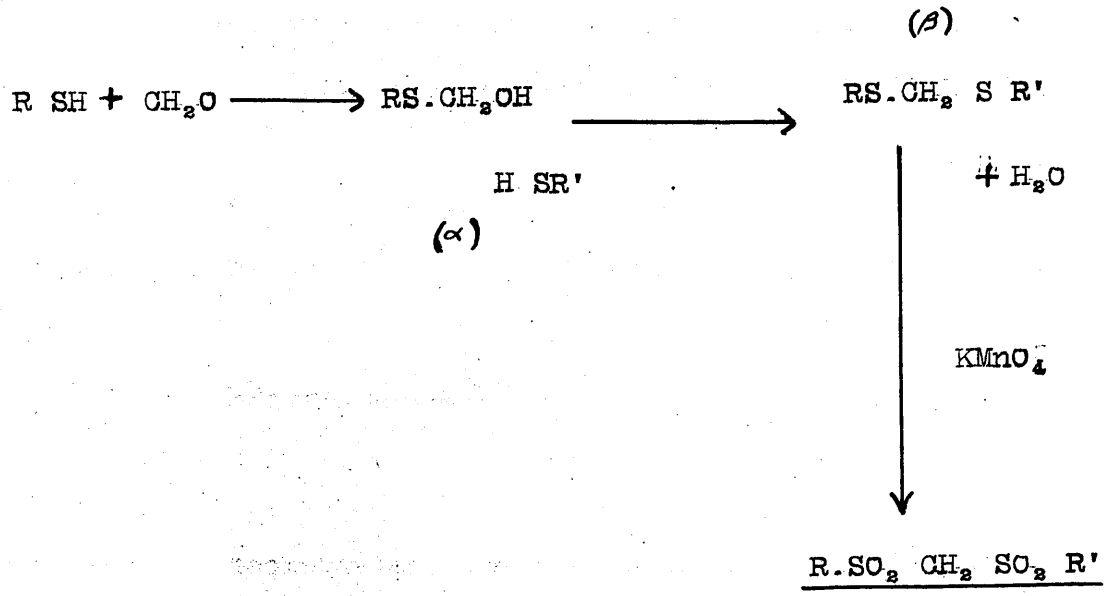
(11) Introduction of a third sulphonyl radicle.

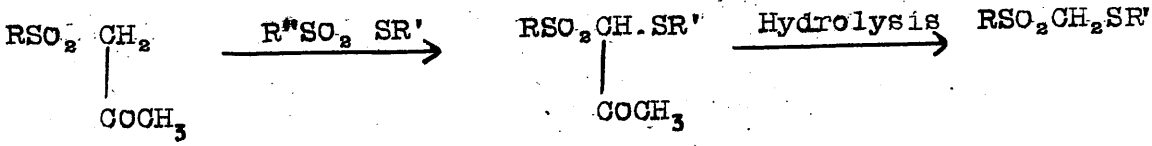


Section 1.

Two general methods are practicable, the old, quick, simple and most disgusting, the new, expensive and perfectly innocuous. They are most easily appreciated schematically :-

Scheme 1.





Scheme 2.

The real weakness of the first method is (α) which could not be purified, consequently (β) may sometimes be contaminated with the two symmetrical disulphides

$R.S.CH_2.S.R.$ $R'S.CH_2.S.CH_2R'$

The fractional distillation of these mixtures caused such complaint as to necessitate scheme (2)

Smiles found that the group S-Aryl may be introduced into Keto-methylene compounds by reaction with disulphoxides :-

$$R.CO.CH_2.CO.R \xrightarrow{PhSO_2SPh} R.CO.\underset{\underset{S\ Ph}{|}}{CH}.CO.R$$

Scheme (2) incorporates several important innovations.

(a) the application to sulphonyl-acetones and sulphonyl acetic esters :-

$$R.SO_2.CH_2.CO\ R \xrightarrow{PhSO_2SPh} R.SO_2\ \underset{\underset{S\ Ph}{|}}{CH}\ CO\ R$$

$$R.SO_2.CH_2\ COOEt \longrightarrow RSO_2\ \underset{\underset{S\ Ph}{|}}{CH}\ COOEt$$

(b) the introduction of the-SMe group into bis-sulphonyl methanes by the use of the methyl esters of phenyl and p-toluene thio-sulphonic acids.

$$R.\,SO_2.\,CH_2\,SO_2.\,R \xrightarrow[\text{or } CH_3C_6H_4SO_2SCH_3]{C_6H_5SO_2SCH_3} R.\,SO_2\,\underset{\displaystyle SCH_3}{\overset{\displaystyle |}{CH_2}}\,SO_2\,R$$

When the two innovations were combined, a new type of Exchange Reaction was discovered :-

$$C_6H_5SO_2.CH_2.COCH_3 \xrightarrow{CH_3C_6H_4SO_2SCH_3} C_6H_5SO_2.\underset{\displaystyle SCH_3}{\overset{\displaystyle |}{CH}}.COCH_3$$

Expected.

$CH_3C_6H_4SO_2SCH_3$

$\downarrow$

$$CH_3C_6H_4SO_2\underset{\displaystyle SCH_3}{\overset{\displaystyle |}{CH}}COCH_3$$

Found.

The study of this Exchange Reaction has developed in several ways, and in so far as relevant to the present work, is discussed in a later section.

Section 11.

Thus, by means of the reactions outlined on page 10, the following bis-sulphonyl methanes were prepared :-

$CH_3SO_2\ CH_2\ SO_2\ C_2H_5$.

$C_6H_5\ SO_2\ CH_2\ SO_2\ CH_3$.

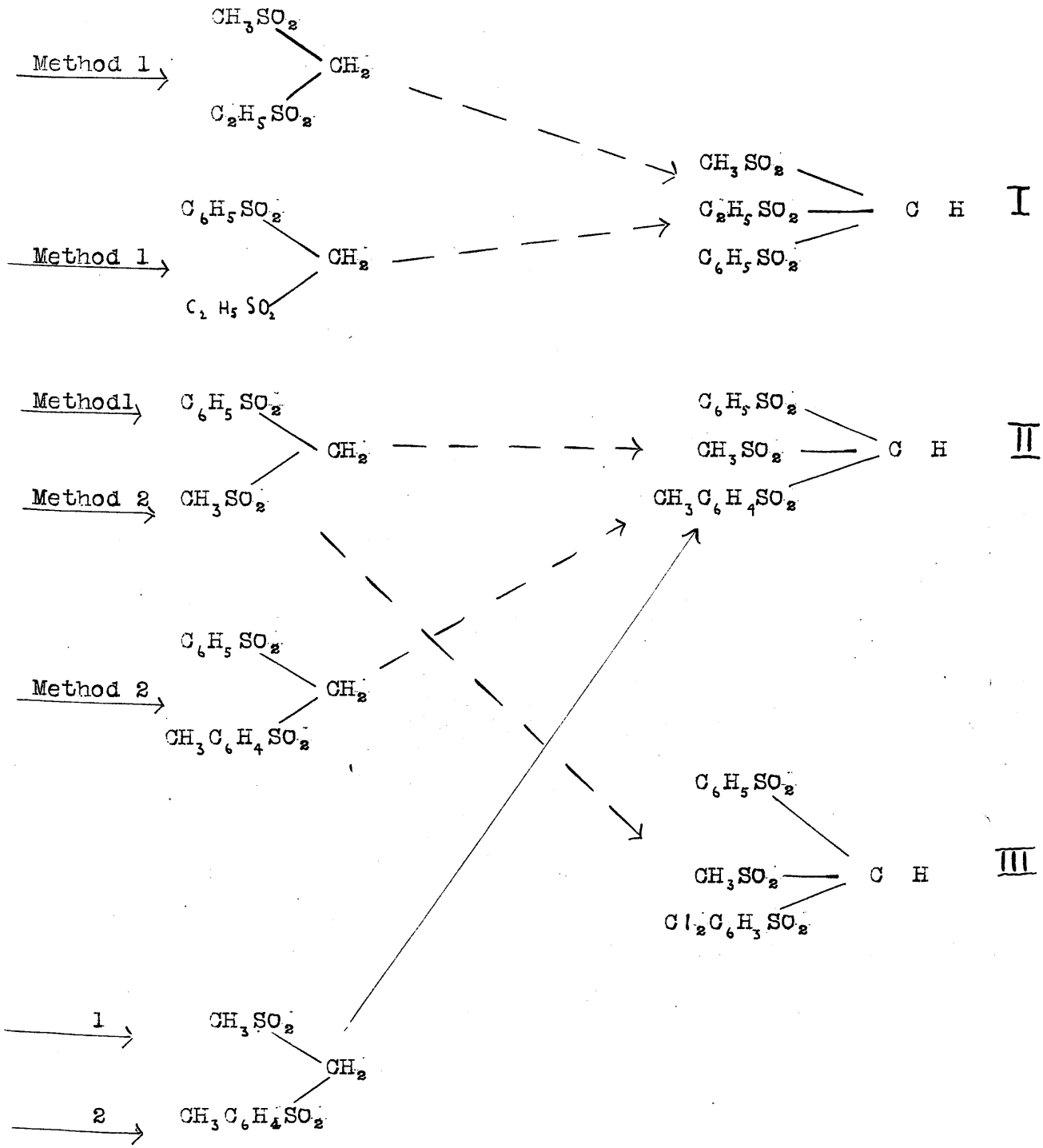
$C_6H_5\ SO_2\ CH_2\ SO_2\ C_2H_5$.

$C_6H_5\ SO_2\ CH_2\ SO_2\ C_6H_4\ CH_3$.

These again reacted with a thiosulphonic ester to yield a sulphide from which another oxidation produced the desired trisulphone

$$R\ SO_2\ CH_2\ SO_2\ R' \xrightarrow{RSO_2SR''} R\ SO_2\ \underset{\underset{S\ R''}{|}}{CH}\ SO_2\ R'$$

The following scheme shews the inter-relationships between the actual compounds examined :


Method 1
CH3SO2
CH2
C2H5SO2
Method 1
C6H5SO2
CH2
C2H5SO2
CH3SO2
C2H5SO2
C6H5SO2
C H
I
Methodl
C6H5SO2
CH2
Method 2
CH3SO2
C6H5SO2
CH3SO2
CH3C6H4SO2
C H
II
Method 2
C6H5SO2
CH2
CH3C6H4SO2
C6H5SO2
CH3SO2
Cl2C6H3SO2
C H
III
1
CH3SO2
CH2
2
CH3C6H4SO2

The trisulphonyl methanes dissolve readily in solutions of organic bases. The Cinchonine salts are rather too soluble to form good crystals. From I, however, well formed Brucine and dextro Hydroxyhydrindamine salts were obtained.

Active hydroxyhydrindamine has the double advantage of being a strong base and equally accessible in dextro and laevo form. This makes a particularly delicate test possible. A salt obtained from d-hydroxyhydrindamine and the trisulphonyl-methane may be one of three :-

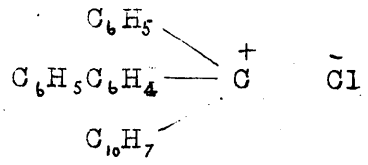
d H H l acid
1

d H H d acid
11

d H H dl acid
111

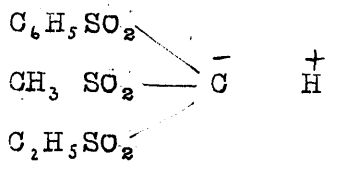
Now in 1 and 11 it is quite possible that the most careful separation of the base might bring about racemisation of the acid. Therefore the base was not removed, but its activity annulled by the addition of an equal amount of laevo base, and the solution examined as quickly as possible. Yet the solution was quite inactive, indicating that the salt obtained was 111. The results with Brucine confirmed this.

My attention was then directed to Dr. Karagunis' thesis.[19] He had examined several similarly substituted tri-aryl methyls, but with the only one which gave a salt suitable for fractionation, he observed no evidence of resolution.



Karagunis

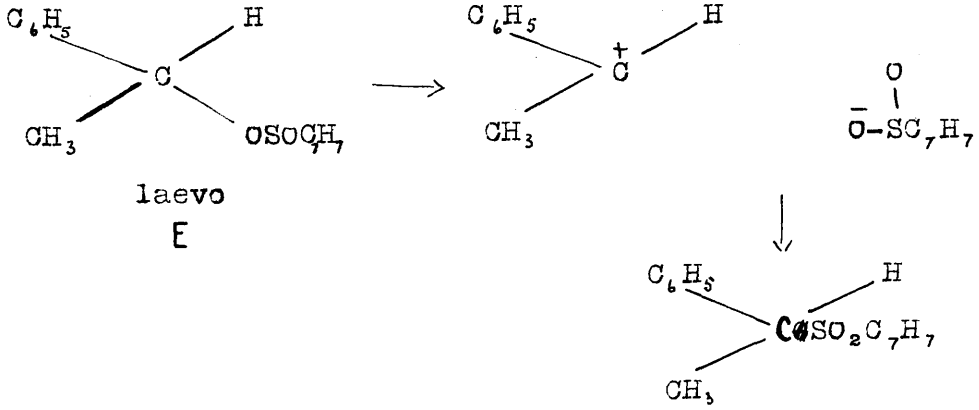
carbon in cation



D.T.G.

anion

Now, while it cannot be denied that these negative results may be due to the particular compounds chosen, or to the bases used to attempt their resolution, there are good reasons for supposing that the life of a carbonium ion in the active state is too fleeting to permit of its isolation. Thus, while Kenyon and Phillips[20] assume that it can exist long enough to influence the course of a reaction, they consider that it is not optically stable in the free state. They cite the active sulphinic ester E which spontaneously changes on standing to the sulphone S The sulphone, obtained in this manner, is always inactive although by another reaction it can, quite readily, be prepared active and kept so. They say that the phenyl methyl carbinyl ion racemises before it combines again.

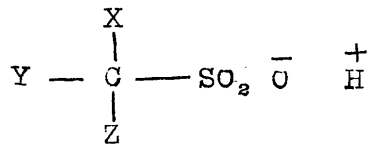


laevo

E

S inactive

Again, while the methane sulphonic acids



are not strictly comparable with the sulphonyl methanes it may not be out of place to mention that Read[21] has found that the one sulphonyl group makes the molecule particularly inclined to racemise.

It appears then that the life of an active carbonium ion will, in the most favourable circumstances, be brief. The two cases mentioned above, combined with the present work on the polysulphonyl methanes indicates that the sulphonyl radicle probably exercises a very unfavourable influence. Consequently, any further experiments to this end must avoid this grouping and seek a carbonium ion among compounds of a completely different type.

There is also a positive reason for considering that further work in this direction on the polysulphonyl methanes would be unprofitable. The experiments with them have shown that their behaviour with solvents is characteristic. They are for the most part insoluble in organic solvents. They dissolve moderately in hot water and they are exceedingly easily soluble in alkaline solutions or solutions of organic bases. Moreover, when a hot aqueous solution of the pure sulphonyl methane (free from any base) is cooled, nothing separates until the solution is moderately acidified with hydrochloric acid. These fact suggest that the solid, on dissolving unites with the hydroxyl ions to form a complex which is much more soluble, and consequently remains in

solution on cooling, until the addition of excess mineral acid, by reducing the hydroxyl ion concentration, brings about the reprecipitation of the undissociated methane

$$H_2O \longleftrightarrow H + \underbrace{OH' \quad HC(SO_2R)_3}$$

(undissociated: insoluble)

$$\updownarrow$$

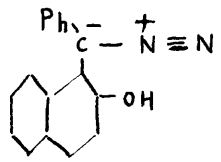
$$H\bar{O}\cdot HC(SO_2R)_3$$

(complex: soluble)

It will be seen at once that bases would favour the formation of such a complex by increasing the hydroxyl ion concentration; and so at no stage, would the central carbon atom be charged, and attached to only three groups. The formation of such a complex is entirely in keeping with the well known reluctance of carbon to depart from the normal 4 co-valent condition, and it explains why no colours have been observed with the sulphonyl methanes such as are characteristic of 'trivalent' carbon. Consequently, even if an active sulphonyl methane were to be isolated, it would not bear on the question initially raised by Frankland.

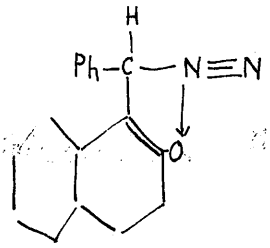
ADDENDUM.

Ray (J.A.C.S. 1932. 295) has just reported the preparation of



As it is crystalline and has $[\alpha]_D$ -420°, it is free from the objections of Noyes' compounds. It is claimed that the fact of its **NOT** being racemised in alkaline solution supports the formula

given. The presence of the β hydroxyl group seems an unfortunate complication, and while the author rejects a mono-molecular cyclic formula :



the absence of molecular weight determinations still leaves open the possibility of a tetrazine. (dimolecular).

THE EXCHANGE REACTION.

$$PhSO_2CH_2COCH \xrightarrow{MePhSO_2SMe} MePhSO_2CH(SMe)COCH + PhSO_2H$$

When the Exchange Reaction was elucidated, it was necessary to re-examine the reactions used in preparing poly-sulphonyl methanes lest the structure assigned to any of them might require revision.

Actually, the structures remain unaffected. The reason is practical. The Exchange Reaction is a mass action effect which leads to an equilibrium mixture of products, usually oily and always difficult to purify. Some of the projected syntheses gave easily purified products, others did not. The former, only, were used. As will be seen below, the easily purified products contain groups which inhibit the Exchange Reaction; while the others contain the very groups which favour it.

The phenomenon was first encountered in attempting to prepare phenyl sulphonyl ethyl sulphonyl methane :

$$C_6H_5SO_2CH_2SO_2C_2H_5$$

from phenyl sulphonyl acetone and ethyl p-toluene thiosulphonate.

The product had, however a persistently low M.P. and considering the ethyl p-toluene thiosulphonate as possibly at fault,* the corresponding methyl compound was synthesised, and as

* a high boiling non-crystalline oil,[22] since obtained crystalline

it was found to be readily crystalline, it was applied to the preparation of :-

$$Ph\ SO_2\ CH_2\ SO_2\ Me$$

Here again, results were disappointing, for the most carefully purified materials gave only a very moderate yield of the thio-acetone

$$R\ SO_2\ \underset{\displaystyle SMe}{\overset{\displaystyle |}{CH}}\ COMe$$

Moreover, the analyses were low in sulphur, high in carbon not only in X, but in Y and Z which are produced from it by hydrolysis and subsequent oxidation

$$R\ SO_2\ \underset{\displaystyle S\ Me}{\overset{\displaystyle |}{CH}}.\ COMe \qquad X$$

$$R\ SO_2\ \underset{\displaystyle S\ Me}{\overset{\displaystyle |}{CH_2}} \qquad Y$$

$$R\ SO_2\ \underset{\displaystyle SO_2\ Me}{\overset{\displaystyle |}{CH_2}} \qquad Z$$

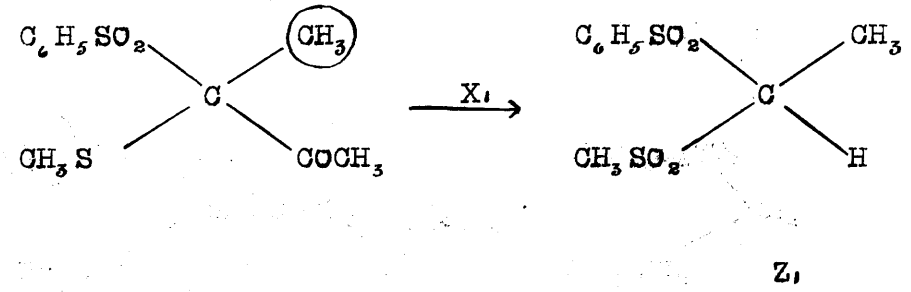
The analytical data, in fact corresponded with one extra CH_2 group in X and Y and Z. A Sample of phenyl sulphonyl methyl sulphonyl methane was accordingly prepared by the old method :-

$$Ph\ SH + CH_2O \longrightarrow \underset{\displaystyle H\ SMe}{\overset{\displaystyle |}{Ph\ S\ CH_2OH}} \longrightarrow Ph\ S\ CH_2\ SMe \searrow$$

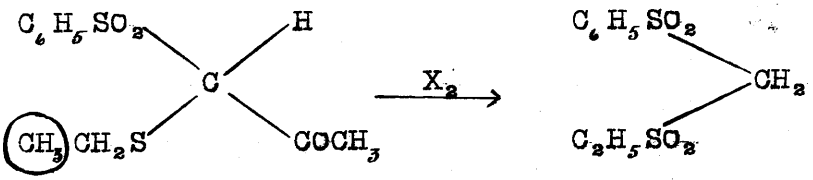
$$PhSO_2CH_2SO_2Me.$$

This gave correct analytical results, and melted a few

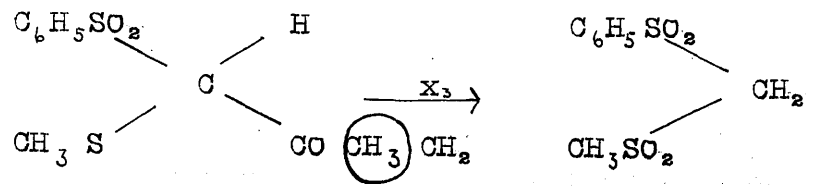
degrees higher than Z. Mixed with Z it gave a distinct depression. There are four places where the extra CH_2 may conceivably be :-



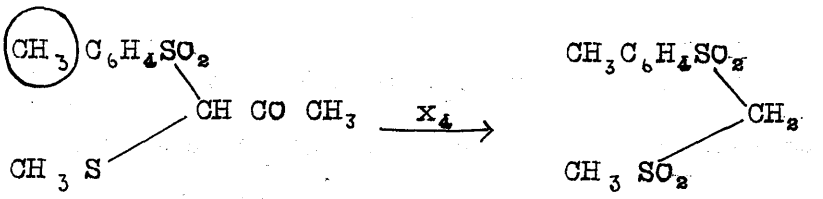
Z_1



Z_2



Z_3



Z_4

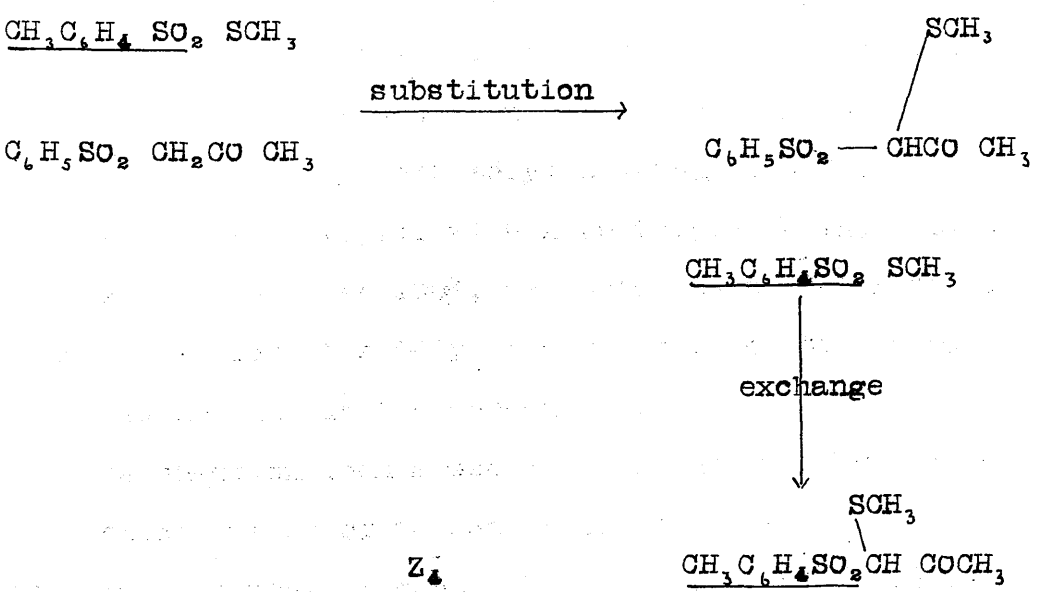
X_1 Methyl toluene thiosulphonate might not only insert the SCH_3 group but also methylate the product.[23] The analytical results are not, however, to be explained thus, because the compound is soluble in alkali as X_1 would NOT be; and X_1 would lead to Z_1 which was independently synthesised and found different.

X_2 It seemed possible that purification of methyl toluene thiosulphonate from ethyl alcohol, might have converted it into the ETHYL ester and consequently inserted a ThioETHYL group. This is turn was disproved by preparation of a sample entirely

with methyl alcohol. Moreover, X_2 would lead to Z_2 which is known and quite different.

X_3 Hydrolysis of the acetyl group would mean the disappearance of the anomaly in Y_3 and Z_3 which is not so.

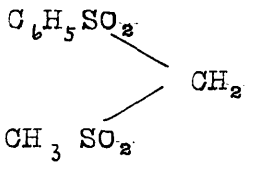
X_4 Finally, Mr. J.D. Louden pointed out that the phenyl sulphonylacetone and methyl toluene thiosulphonate had possibly undergone two reactions :-



This last has been fully confirmed :-

(1) by independent synthesis of Z_4.

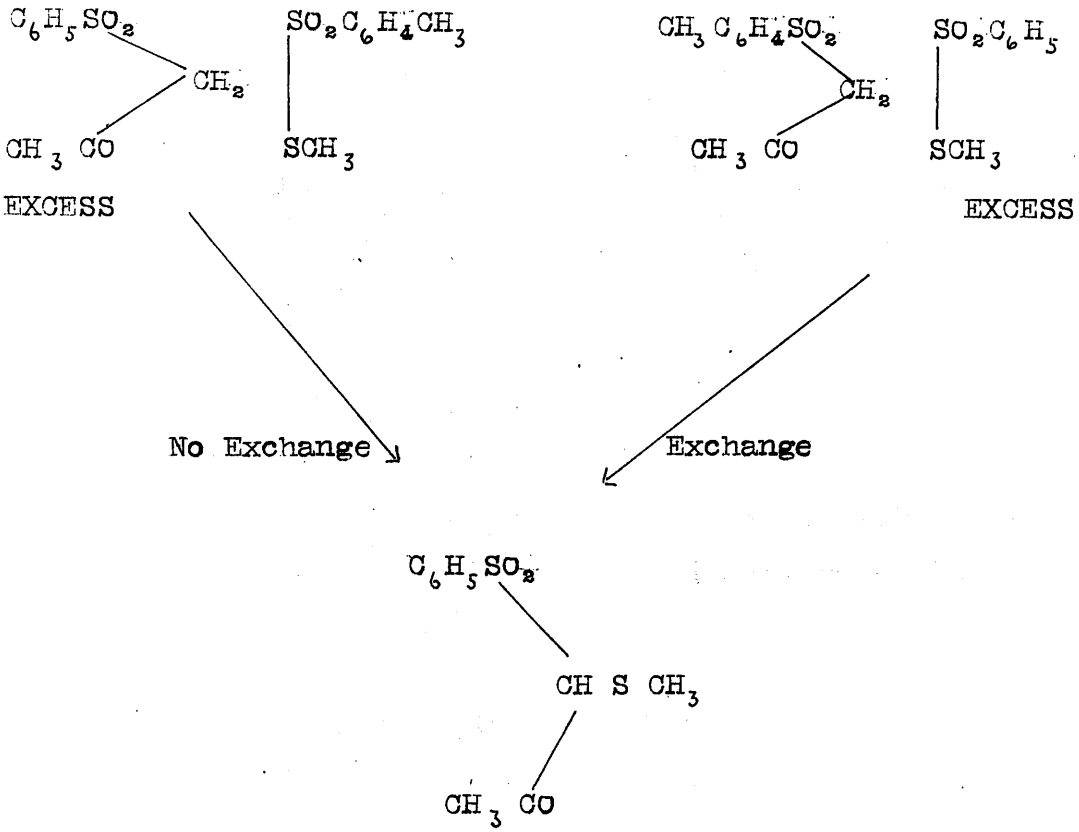
(2) If phenyl sulphonylacetone is treated with methyl phenyl thiosulphonate it should yield the originally "expected" products X - Y - Z which would not have an additional methyl group - and Z of this series should be



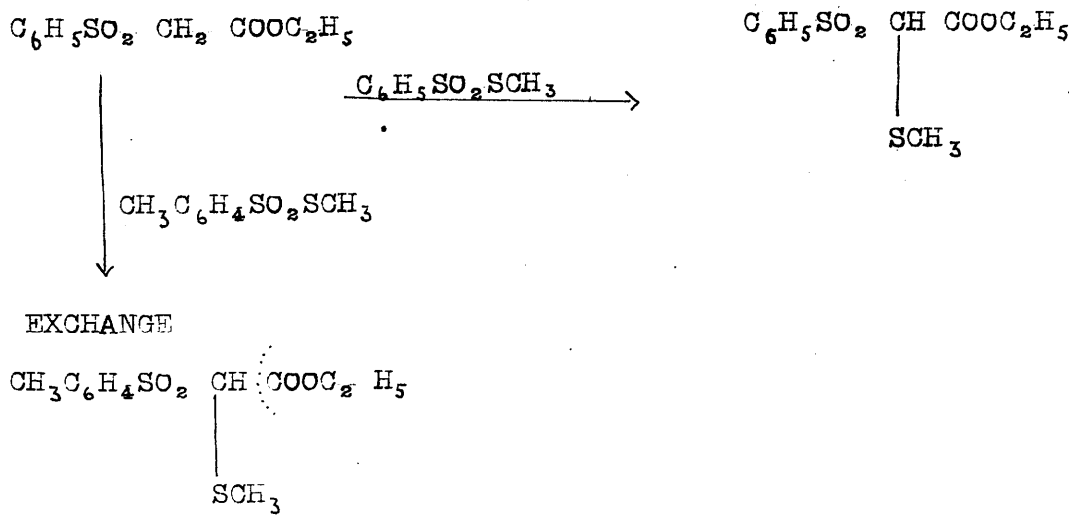
Analysis confirmed the former and direct synthesis the latter.

(3) Tolyl sulphonylacetone and methyl tolyl thiosulphonate should, and did, yield ~~rather~~ readily purer specimens of the originally "found" X_4 - Y_4 - Z_4. Further, in the original experiments, even most carefully purified compounds gave much oily by-products such as was not observed when the radicle in both reactants was phenyl sulphonyl, or both tolyl sulphonyl. This oil was probably a mixture of X (phenyl), with X (p.tolyl), - indicating that the exchange had not been 100%, as indeed is to be expected, for the actual isolation of a tolyl product may be attributed to its lesser solubility in the common solvents.

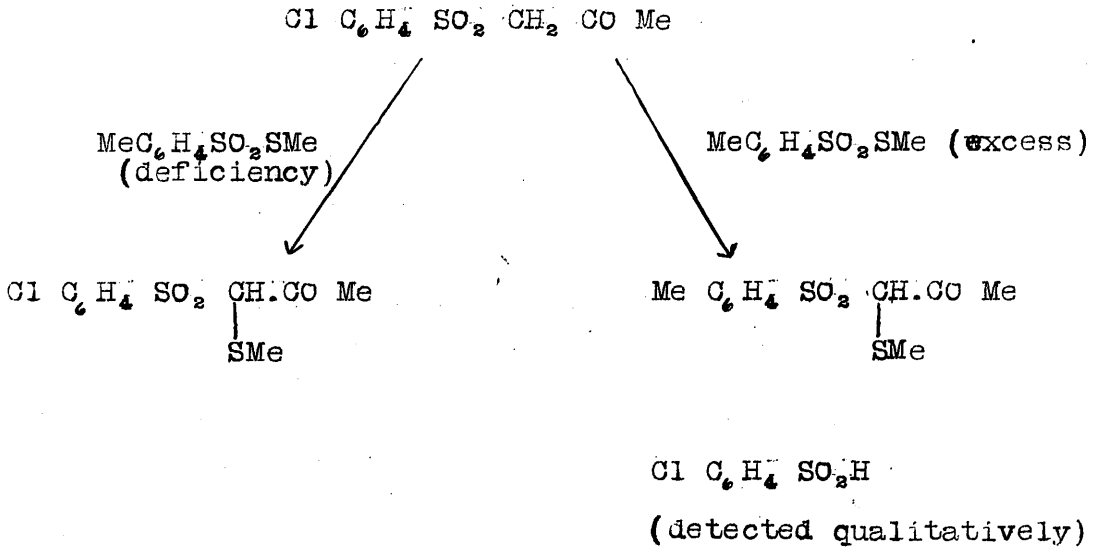
The question then arose whether the exchange was due to a mass action effect or to some Polarity effect.
The very fact that it should be evident at all with radicles so similar as phenyl sulphonyl and tolyl sulphonyl rather favours the former. That is confirmed by two simple reactions :-



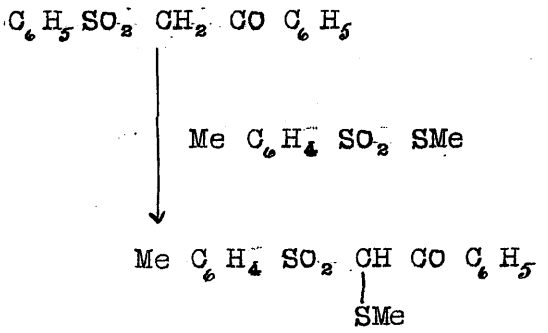
Exactly similar exchange occurs with phenyl sulphonyl acetic ester :-



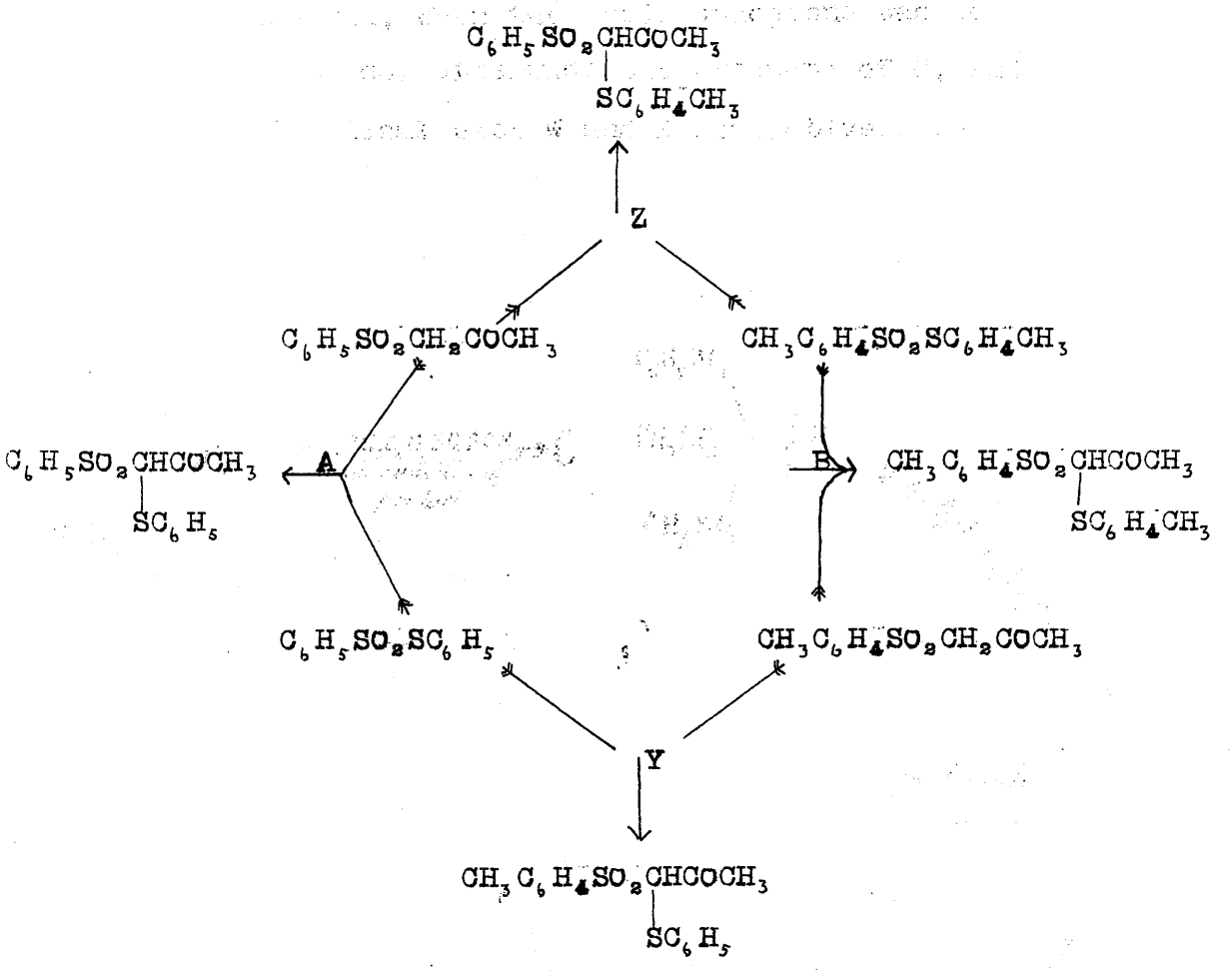
And with 4 chloro phenyl sulphonyl acetone and methyl p-toluene thiosulphonate.



And with phenyl sulphonylacetophenone



Exchange does not take place when the disulphoxide is purely aromatic, as indicated in the following scheme



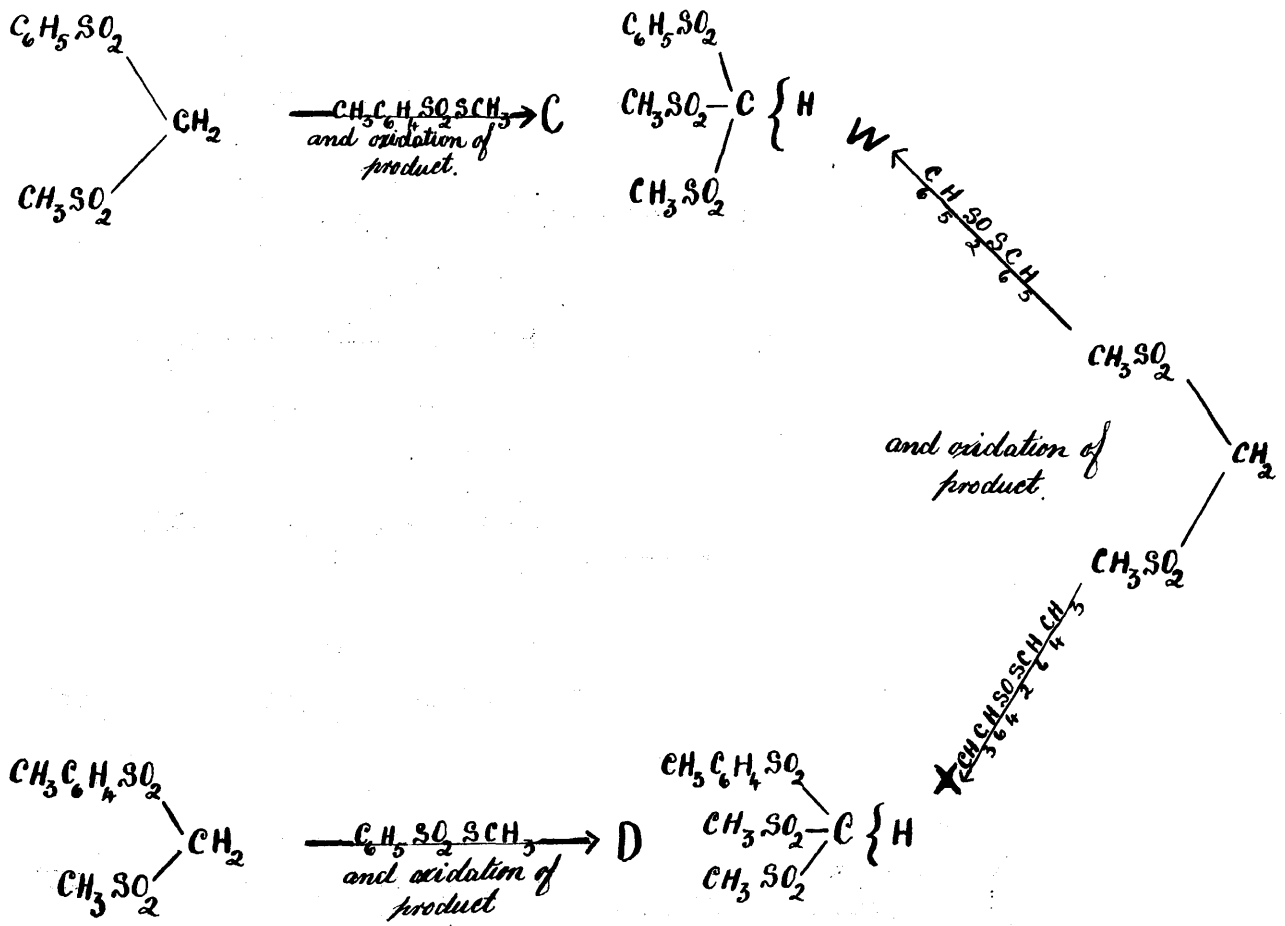
In **A** the radicles must be both phenyl No EXCHANGE

In B " " " " " p-tolyl POSSIBLE.

In Y Exchange would have produced **A**, which was not found.

In Z " " " " B, " " " " .

No exchange occurred, when the sulphonacetone was relpaced by a disulphonyl methane, otherwise the products of C, and D, would not have been identical with W and X respectively :-



It remains now to mention three other projected syntheses for trisulphones, and to consider what light is thrown on the mechanism of the Exchange Reaction by the unexpected products which were isolated :

I. $R\,SO_2\,CH(Br)\,SO_2\,R + AgSO_2Ph \longrightarrow R\,SO_2\,CH(SO_2Ph)\,SO_2\,R$ (expected)

(found) $R\,SO_2\,CH_2\,SO_2\,R$

This is quite parallel to Trüger's observation[25]

$R\,SO_2\,C(CN)(Br)_2 + \varphi SO_2\,H \longrightarrow R\,SO_2\,CH_2\,CN$

II. $R\,SO_2\,CH_2\,SO_2\,R \xrightarrow{RSO_2Cl} R\,SO_2\,CH(SO_2R)\,SO_2\,R$ Expected

found $R\,SO_2\,CH(Cl)\,SO_2\,R$

III. $Ph\,SO_2\,CH_2\,SO_2\,Me$ (M) $\xrightarrow{MeC_6H_4SO_2SO_2C_6H_4Me}$ $Ph\,SO_2\,CH(SO_2\,C_6H_4Me)\,SO_2\,Me$ Expected

(F) $Ph\,SO_2\,CH(S\,C_6H_4Me)\,SO_2\,Me$

found

The explanation of III is that the disulphone first underwent hydrolysis:

$$CH_3C_6H_4.SO_2.SO_2.C_6H_4CH_3 + H_2O \longrightarrow CH_3C_6H_4SO_2H + CH_3C_6H_4SO_3H$$

Now, it is well known that sulphinic acids undergo auto oxidation-reduction with the formation of thiosulphonic esters :-

$$3CH_3C_6H_4SO_2H \longrightarrow CH_3C_6H_4SO_2SC_6H_4CH_3 + CH_3C_6H_4SO_3H + H_2O$$

(D)

The reaction of D with the disulphonyl methane M results in the formation of F -- this is of course the way in which F was originally prepared (see p. 56).

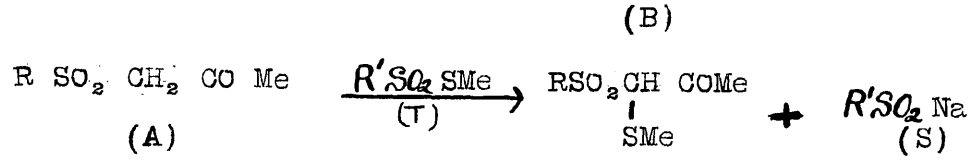
The similarity between the formulae of thiosulphonic esters $R\,SO_2\,SMe$ and sulphonic esters $R\,SO_2\,OMe$ suggested that a methoxyl group might be introduced into the sulphonyl methanes with the latter reagent. On the other hand, as that reagent is commonly used for methylating,[23] it was not altogether unexpected that phenyl sulphonyl methyl sulphonylmethane was methylated to :-

$$Ph\,SO_2\,CH_2\,SO_2\,Me \xrightarrow{MeC_6H_4SO_2OMe} Ph\,SO_2\,CH(OMe)\,SO_2\,Me$$

possible ?

found $Ph\,SO_2\,CH(Me)\,SO_2\,Me$

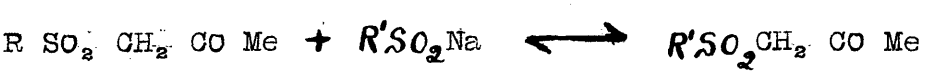
When the Exchange Reaction was first discovered, it seemed possible the first action was normal substitution



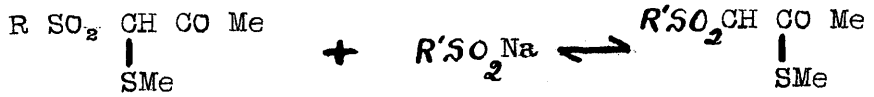
followed by an exchange of R SO_2 for $R'SO_2$.

This latter might occur in one of 3 ways.

(a) Double decomposition between the liberated sulphinic acid (S) and the still unattacked sulphonyl acetone (A)



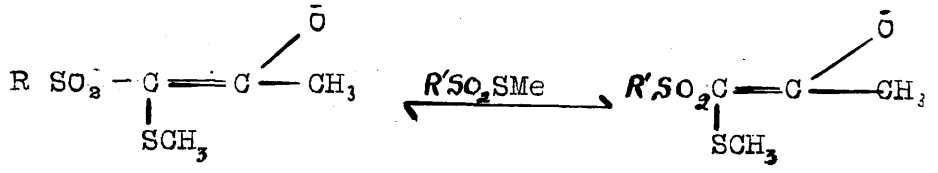
(b) Double decomposition between (S) and the newly formed substitution product (B)



Actual tests with (A) or (B) and $R'SO_2Na$ were, however, negative.

(c) There remained, therefore, the possibility of exchange between (T) and (B). This actually was realised, but only in an alkaline medium, indicating that the exchange involves the negative ion of (B).

The simplest formulation of the exchange is to suppose the thiosulphonic ester to react reversibly with the ion of the enol form of the sulphonyl acetone



This formulation of the reaction is in accord with the fact that Exchange does not occur with bis sulphonyl methanes :

$$R\ SO_2\ CH_2\ SO_2\ R$$

for, as has been already indicated, the sulphone group does not enolise. The enolisation of the sulphonyl acetones may explain why it was not found possible to chlorinate them with p-toluene sulphonyl chloride (contrast II, page 30) although

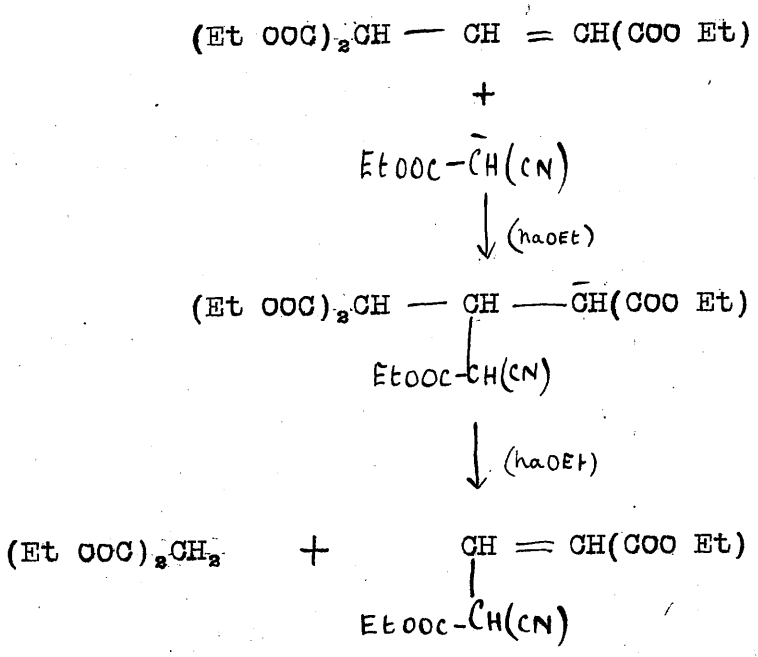
$$R\ SO_2\ \underset{\displaystyle Cl}{\underset{|}{CH}}\ CO\ Me$$

is known to be capable of existing.

The investigation of the phenomenon where R is phenyl and R' is tolyl has advantages as well as drawbacks. On the one hand, the discrepancies in the analyses being only just large enough not to be ignored, the phenomenen was very nearly overlooked, and was not considered established until it was checked by a series of mixed melting point determinations. On the other hand the phenyl and p-tolyl groups are chemically so similar that the demomstration of the interconversion of a derivative of the one into the other was not complicated by any polarity consideration such as might intervene if R' were dichlorphenyl or nitrophenyl.

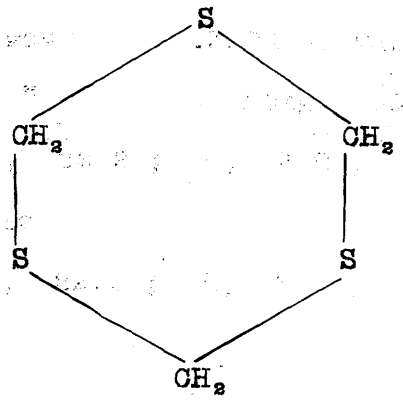
Incidentally, it has subsequently been found that exchange can occur, or can be suppressed, when R = phenyl and R' = p-chlorophenyl.

Finally, the Exchange Reaction has at least a formal similarity to a remarkable reversed Michael condensation discovered by Ingold[26]:

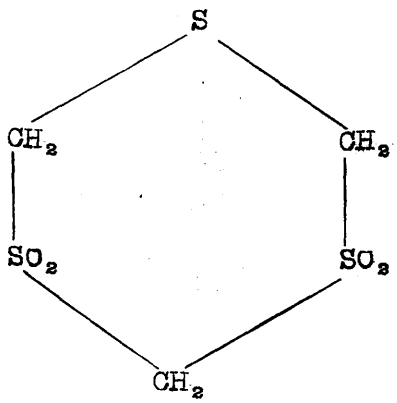


EXPERIMENTAL.

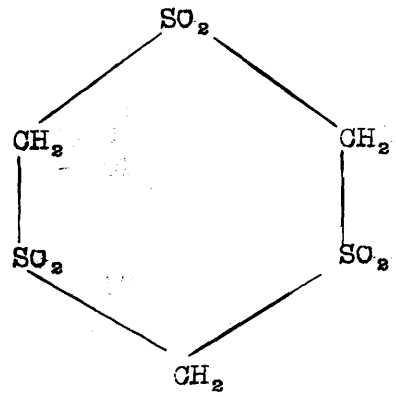
HALOGENATED SULPHONES DERIVED from



The disulphone sulphide 1 and the trisulphone 11 were prepared as described by Camps [12]. He methylated them with methyl iodide. Methyl sulphate was found to act more smoothly.



1



11

Methylation of 1.

A cooled solution of 1 in the minimum alkali was

treated with the requisite amount of dimethyl sulphate. The mono-methyl derivative 111 crystallised out in 75% yield. It decomposed at a high temperature without melting and after recrystallisation from hot water and sublimation in a vacuum:-

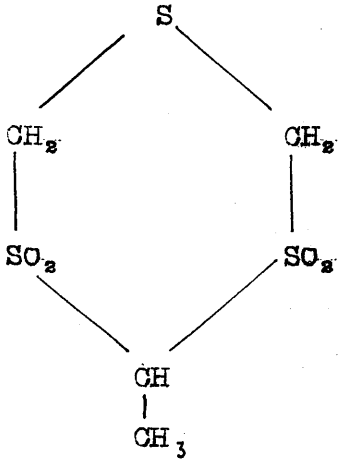
.1104 g. gave .3594 g. $BaSO_4$.

5·32 mg. " 4·33mg. CO_2 and 1·87mg. H_2O

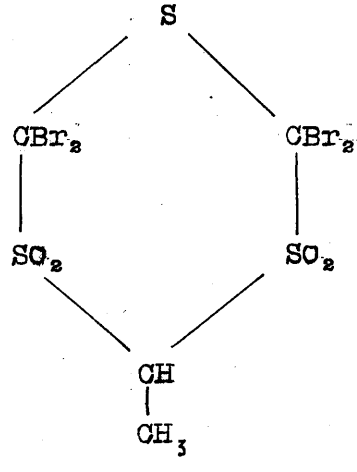
whence C, 22.2 ; H, 3.9 ; S, 44.6

$C_4H_8O_4S_3$ requires

C, 22.2 ; H, 3.7 ; S, 44.4%.



111



1V

Bromination of 111.

The mono-methyl compound was warmed to 50° with a solution of bromine in KBr and 10% acetic acid. After several days the undissolved crystals were removed. The tetrabromo

derivative IV crystallised from the filtrate. Recrystallised from glacial acetic acid, m.p. 205°.

The ordinary Carius proceedure :-

.0754 g.	gave	.0965 g.	$BaSO_4$.	S, 17.6%.
.1028 g.	"	.1420 g.	$AgBr_2$	Br, 58.7%

special, at 310 :-

.1065 g.	gave	.1488 g.	AgBr.	Br, 59.3%.
.0974 g.	"	.1360 g.	AgBr.	Br, 59.5%.

Bromine was more easily and accurately estimated by warming the compound with a concentrated alkaline solution of pure sodium sulphite, cooling, diluting, acidifying and precipitating with silver nitrate.

.1256 g.	gave	.1772 g.	AgBr.	Br, 60.0%.
IV	requires	S, 18.0	Br, 60.0%.	

Methylation of the Trisulphone II.

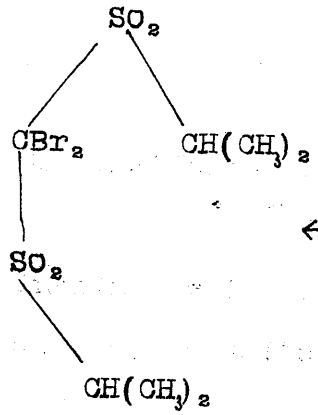
Camps obtained mixtures of the dimethyl, and trimethylated sulphones with methyl iodide.

With dimethyl sulphate.

The potassium salt (27 g.) suspended in water containing sodium hydroxide (4 g.) was treated with dimethyl sulphate (19 c.c) The methylated sulphone IV, which crystallised out, was purified

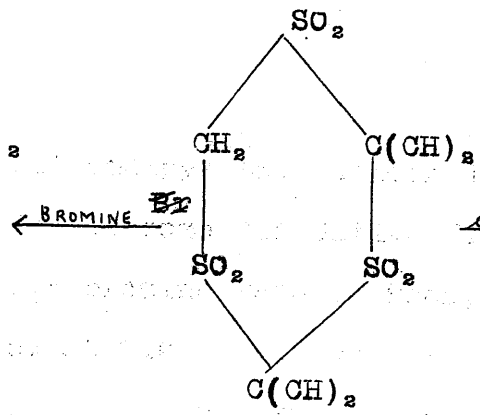
from hot water, yield 50%.

.1010 g. gave .2410 g. $BaSO_4$. S, 32.7.



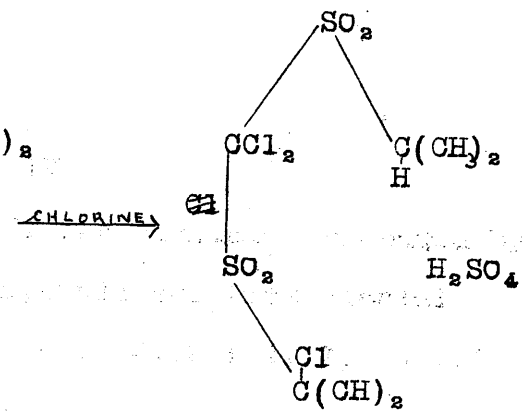
VI.

requires Br.41.9%.



IV.

requires S,33.5%.



V.

requires Cl,32.5%

Chlorination of Tetramethyl trisulphone IV.

The trisulphone was insolated for several weeks with chlorine water till the product was easily soluble in chloroform. After recrystallisation from glacial acetic acid it melted at 280 - 285°. The presence of chlorine was evident from the copper wire test, but no silver chloride was formed in a Carius tube at 280 and even at 340 decomposition was incomplete.

Estimation of halogen was done with alkaline sulphite :-

.1320 g.	gave	.1717 g.	AgCl.	32.1% Cl.
.1126 g.	gave	.1460 g.	"	32.0 " "
.1214 g.	gave	.1580 g.	"	32.1 " "

Bromination of Tetramethyl trisulphone IV.

The dibromo derivative VI was similarly prepared by insolating IV with bromine water. Recrystallised from glacial acetic, it melted at 246°. (Found : Br, 41.2 ; 41.7, 41.4%

VI $C_7H_{14}O_4Br_2S_2$ requires Br, 41.4%.

Ethylene Dimercaptan.

Ethylene dibromide (20 c.c.), water (20 c.c.), sodium thiosulphate (100 g.), and alcohol (100 c.c.) were mechanically shaken for 6 hours at 50 - 60°. The stiff pasty product was collected, boiled with excess hydrochloric acid, and distilled in steam, yielding 9 g. of the mercaptan, b.p. 144 . If the hydrolysis is conducted with alkali, no mercaptan is formed.

Condensation of Ethylene Dimercaptan with Formaldehyde.

The mercaptan was slowly added to formalin solution, containing a trace of hydrochloric acid, below 25 . The clear solution, when gently warmed, suddenly became turbid with separation of 1 : 3-dithiolan and its polymeride. The former was distilled in steam and purified as described below.

The polymeride, m.p. 105 - 110°, after being washed with ether, was practically insoluble in any organic solvent; it dissolved with effervescence in nitric acid, giving a red solution (Found; C, 34.1 ; H, 6.1. $(C_3H_6S_2)_n$ requires C, 34.0 ; H, 5.7%).

1 : 3-Dithiolan, was more conveniently obtained by treating sodium ethylene thiosulphate, prepared as described above, with a mixture of hydrochloric acid and twice the calculated amount of formalin. Steam distillation furnished a 50 - 60% yield of the dithiolan, which was purified by refluxing it for several hours with aqueous alkali ; it then boiled at 175°/ 760 mm. and 61°/11 mm. and had d 1.259, n 1.5975, whence $[R_L]_D$ =29.7 (calc., 29.8) (Found : C, 34.2 ; H, 5.8. $C_3H_6S_2$ requires C, 34.0 ; H, 5.7%).

.3661 g. depressed the F.P. of 17.6 g. benzene 0.950°.
.7322 g. " " " " 22.0 g. " 1.536°.

whence Mol. Wt. 112, 111.
Calc. 106.

It yielded a mercurichloride, m.p. 119°, on treatment with mercuric chloride.

Dithiolan Disulphone was prepared by adding perhydrol (50 c.c.) in glacial acetic acid (40 c.c.) to a solution of redistilled dithiolan (10 c.c.) in an equal bulk of the same solvent, the addition being just fast enough to maintain the temperature 40 - 50°. After standing overnight the excess perhydrol was destroyed with sulphurous acid and the solution evaporated to crystallisation. Yield 80%. The same product, m.p. 224°, was obtained by

Baumann and Walter's method[31] with permanganate.

2 ; 2 dichloro 1 ; 3 dithiolan disulphone was prepared by chlorinating, in sunlight, an aqueous suspension of the disulphone below 50 . Recrystallised from benzene, it melted at 233° ; yield 50%. (Found : Cl, 29.5 . $C_3H_4O_4Cl_2S_2$ requires Cl, 29.8%)

2-bromo 2-methyl 1 ; 3-dithiolan disulphone was prepared by brominating the 2-methyl disulphone in warm water. Recrystallised from hot water. M.P. 248°. (Found ; Br, 30.0. $C_4H_7O_4BrS_2$ requires Br, 30.3%).

1 : 3-Dithiolan Monoxide.

Perhydrol (9 c.c.) in 20 c.c. of glacial acetic acid was added very slowly to specially purified 1 ; 3-dithiolan (10 c.c) in 20 c.c. of glacial acetic acid. After several days, the solvent was removed below 40°, first at 11 mm. and finally at 1 mm. (neglect to remove every trace of solvent at as low a temperature as possible causes complete decomposition in the subsequent distillation) and the residue was distilled over a trace of magnesium carbonate, giving 8 g. of an oil, b.p. 115 - 120°/ 1 mm. (Found ; C, 30.1 ; H, 5.3 ; $C_3H_6OS_2$ requires C, 29.5 ; H, 5.0%)

.4748 g. depressed the F.P. of 15.0 g. water 0.482°.

whence Mol. Wt. 118

Calc. 122.

The monoxide is miscible with water, and is decomposed by warm hydrochloric acid into dithiolan (identified by its mercurichloride, m.p. 119°) and a dioxide, m.p. 134°. (Found; C, 26.3; H, 4.7, 4.3. $C_3H_6O_2S_2$ requires C, 26.0; H, 4.4%). It is insoluble in all the usual solvents, including aqueous alkali.

With platinic chloride, an aqueous solution of dithiolan monoxide yields a flocculent precipitate, which may be recrystallised from hot water; m.p. 146 - 150° (decomp.) (Found; C, 14.0; H, 2.7; Cl, 20.3; Pt, 36.7. $\left[\left((C_3H_5S_2)O\right)_2Pt\right]PtCl_6$ requires C, 13.7; H, 1.9; Cl, 20.1; Pt, 37.0 %).

With methyl iodide, dithiolan monoxide yields a methiodide, m.p. 96°

.1290 g. gave .1150 g. AgI.

whence I 48.0%

$C_4H_9OIS_2$ requires I 48.1%

1; 3-Dithian.

Trimethylene dibromide (30 c.c.), sodium thiosulphate (120 g.), and alcohol (100 c.c.) were shaken at 60° for 2 days. The solid which separated was distilled in steam with formalin and hydrochloric acid, and the distillate extracted with ether. The dithian crystallised readily and melted at 54°.

.1190 g. gave .1762 g. CO_2 and .0764 g. H_2O

.1082 g. " .1588 g. " " .0640 g. "

whence C, 40.1 ; 40.0 ; H, 7.1 ; 6.6

$C_4H_8S_2$ requires C, 40.0 H, 6.7%

On oxidation with perhydrol in glacial acetic acid, it gave Autenrieth and Wolff's disulphone,[24] m.p. 330°, in almost quantitative yield.

Preparation of Disulphonyl Methanes.

Method 1 (page 10)

$R\,SO_2\,CH_2\,SO_2\,R'$

The disulphones were prepared by shaking the less reactive mercaptan with the calculated amount of 40% formalin solution (estimated by Ronijn's[33] method) and warming the mixture till a homogeneous liquid was obtained. The more reactive mercaptan was then added, and the whole agitated with concentrated hydrochloric acid. Even when preparing the symmetrical disulphones ($R = R'$) it is advantageous to add the mercaptan thus in two stages, lest the heat generated cause loss (methyl mercaptan[34] b.p. 6°)

The oil which separated was fractionated with a Widmer column and the appropriate fraction oxidised with permanganate.

Method 11.

The disulphoxide and the sulphonylacetone or sulphonylacetic ester[35] were warmed in alcoholic solution for several hours with sodium ethoxide (calc. amount) ; or with solid anydrous sodium carbonate until it had all dissolved. The alcohol was evaporated, the solution made alkaline if necessary, any insoluble impurity removed with ether, and the required product

precipitated from the aqueous solution with acetic acid. If desired, the sulphinic acid which was similtaneously formed could be removed from the filtrate with mineral acid. The oxidations were conducted by shaking with cold acid 2½% permanganate solution, or with perhydrol in acetic acid. In the latter case any excess was destroyed with sulphurous acid before the product was worked up.

Bis(ethylthio)methane was prepared by Claesson[36] from methylene iodide, and by Baumann[37] from chloroform, and sodium mercaptide, but it is much more satisfactorily obtained from 40% formalin (20 c.c.) and ethyl mercaptan (25 g.). The first runnings are ethyl disulphide, evidently produced by the reaction $CH_2O + 2C_2H.SH = CH_3.OH + C_2H_5.S:S.C_2H_5$. The main fraction, b.p. 182 - 184°, is the required disulphide (yield 75%).

The corresponding disulphone, m.p. 104°, was obtained in practically theoretical yield by oxidation with 1% permanganate solution. The dibromo- and the dichloro-derivative, m.p. 131° and 98° respectively, were obtained as described by Baumann.

Bis(methylsulphonyl)methane also has been obtained by Baumann[38] in a roundabout way from formaldehyde and hydrogen sulphide. It is much more easily obtained by condensing methyl mercaptan with formaldehyde and oxidising the product (b.p. 145 - 150°) as above. The disulphone, m.p. 142°, and its dibromo-derivative, m.p. 234°, as Baumann states, were obtained; the dichloro-derivative melts at 152°.

.1626 g. gave .1950 g. AgCl. whence Cl = 29.7

$C_3H_6O_4Cl_2S_2$ requires Cl = 29.4 %.

Bis(methylsulphonyl)ethane was obtained from methyl mercaptan and acetaldehyde. The disulphide boils at 156 - 158°.

.0989 g. gave .1418 g. CO_2 and .0715 g. H_2O.

whence C, 39.2 ; H, 8.05.

$C_4H_{10}S_2$ requires C, 39.4 ; H, 8.2%

The disulphone (permanganate) has m.p. 122°

.0926 g. gave .0872 g. CO_2 and .0452 g. H_2O.

.1014 g. " .0966 g. " " .0442 g. "

whence C, 25.9, 26.1 ; H, 5.4, 4.9.

$C_4H_{10}O_4S_2$ requires C, 25.8 ; H, 5.4%.

The monoiodo-derivative was obtained by treatment of the disulphone with potassium iodide and iodate[39] in acetic acid ; m.p. 225 .

.1278 g. gave .0978 g. AgI whence I 41.3

.1059 g. " .0806 g. " " I 41.1

$C_4H_9O_4IS_2$ requires I 40.7%.

Methylthioethylthiomethane.

Ethyl mercaptan (1 vol.) and formalin (1 vol.) were heated at 40 - 60° till the liquid was homogeneous. Then to the ice cooled product methyl mercaptan (1 vol.) and a few drops of hydrochloric acid were added and the mixture shaken. When the turbid liquid had cooled, the oil layer was washed with alkali, dried and distilled with a column.

Fraction 1 110 - 155° 6 g. (mainly $CH_3S\ SCH_3$ 112°, $(CH_3S)_2CH_2$ 147°, and $C_2H_5S\ SC_2H_5$ 153°.).

Fraction 11 156 - 180° 20 g.

" 111 above 180° 5g. $(C_2H_5S)_2CH_2$ 183.

Fraction 11 on refractionation gave a main fraction b.p 163 - 167°.

3.99 mg. gave 5.655 mg. CO_2 and 2.94 mg. H_2O

whence C, 39.3 ; H, 8.2

$C_4H_{10}S_2$ requires C, 38.8 ; H, 8.2%.

Methylsulphonylethylsulphonylmethane was obtained by oxidising the disulphide b.p. 163° (10 g.) with acid 2½% permanganate solution. After removing MnO_2 with sulphurous acid, the solution was concentrated to 500 ccs., and next morning the disulphone collected. It was freed from adherent mineral salts by recrystallisation from alcohol and for further purification, sublimed in a vacuum at 110°/ 11 mm. It is soluble in 5 parts of boiling water. M.P. 94 - 95°.

4.475 mg. gave 4.355 mg. CO_2 and 2.33 mg. H_2O.

whence C, 26.6 ; H, 5.8

$C_4H_{10}O_4S_2$ requires

C, 25.8 ; H, 5.4

A mixture with bis(ethylsulphonyl)methane - m.p. 102° - melted below 75°.

Phenylthioethylthiomethane, was obtained from phenyl mercaptan (55 g.) formalin (37 c.c.) and ethyl mercaptan (20 g.). The product was fractionated in vacuo. B.P. 147 - 151°/11 mm. n_D 1.598.

.1010 g. gave .2194 g. CO_2 and .0625 g. H_2O.

whence C, 59.0 ; H, 6.9

$C_9H_{12}S_2$ requires C, 58.7 ; H, 6.6%.

Phenylsulphonyl,ethylsulphonylmethane ; M.P. 110° was obtained in 65% yield by oxidation of the disulphide with permanganate. The same disulphone was originally obtained by Posner, who did not fractionate the disulphide mixture ; his disulphone was consequently a mixture. He obtained it pure only after considerable fractional crystallisation. The same disulphone was also obtained from ethyl phenylsulphonyl-acetate and ethyl p-toluenethiol-sulphonate by oxidising the oil which separated when an aqueous extract of the reaction mixture was warmed. The mother liquor deposited sodium phenylsulphonyl-acetate, indicating considerable loss of ester by hydrolysis. (Found : Na, 10.3. $C_8H_7O_4SNa$ requires Na, 10.3%).

Phenylsulphonyl,methylsulphonylethane.

From phenyl mercaptan (1 vol.) acetaldehyde (1 vol.) and methyl mercaptan (2 vols.) phenylthio - -methylthioethane, b.p. 140 - 145°/10 mm., was obtained

.1030 g. gave .2204 g. CO_2 and .0613 g. H_2O.

whence C, 58.5 , H, 6.6

$C_9H_{12}S_2$ requires C, 58.7 ; H, 6.5%.

This was oxidised to the disulphone, m.p. 104° after recrystallisation from benzene.

5.17 mg. gave 8.29 mg. CO_2 and 2.27 mg. H_2O

whence C, 43.7 ; H, 4.9

$C_9H_{12}O_4S_2$ requires C, 43.6 ; H, 4.9%.

The disulphone was not readily soluble in alkali, and showed no tendency to form a salt with hydroxyhydrindamine.

Phenylsulphonylmethylsulphonylmethane.

Condensation of phenyl mercaptan (55 g.), formaldehyde (37 c.c.), and methyl mercaptan(25 c.c.) gave the disulphide, b.p. 148 - 152°/ 11 mm..

.1134 g. gave .2360 g. CO_2 and .0600 g. H_2O

whence C, 56.8 ; H, 5.9

$C_8H_{10}S_2$ requires C, 56.5 ; H, 5.9%.

The disulphone (yield 50%) had m.p. 147°. (Found : C, 41.1 ; H, 4.7 . $C_8H_{10}O_4S_2$ requires C, 41.0 ; H, 4.4%).

Method 11.

(page 10)

Phenylsulphonyl-p-tolylsulphonylmethane.

Phenylsulphonylacetone (10 g.), p-tolyl disulphoxide (15 g.), and sodium ethoxide gave α-phenylsulphonyl-α- p-tolylthioacetone (12 g.), m.p. 99° (from alcohol)

9.62 mg. gave 14.075 mg. $BaSO_4$

whence S, 20.1.

$C_{16}H_{16}O_3S_2$ requires S, 20.0%.

When this was warmed for a few minutes in alkaline solution the acetyl group was removed and phenylsulphonyl-p-tolylthiomethane was precipitated, m.p. 85° (alcohol)

4.94 mg. gave 10.955 mg. CO_2 and 2.30 mg. H_2O

whence C, 60.5 ; H, 5.2

$C_{14}H_{14}O_2S_2$ requires C, 60.5 ; H, 5.05%.

It gave the disulphonylmethane, on oxidation with perhydrol, in practically theoretical yield ; m.p. 115° (alcohol)

4.91 mg. gave 9.79 mg. CO_2 and 2.09 mg. H_2O

whence C, 54.3 ; H, 4.7

$C_{14}H_{14}O_4S_4$ requires C,54.3 ; H, 4.5%.

Methyl-p-toluene thiosulphonate was obtained by methylating sodium-p-toluene thiosulphonate with methyl iodide (25% yield) or methyl sulphate (60%). M.P. 58° B.P. 193 / 10 mm. (decomp)

5.08 mg. gave 8.84 mg. CO_2 and 2.24 mg. H_2O

whence C, 47.4 ; H, 4.9

$C_8H_{10}O_2S_2$ requires C, 47.5 ; H, 4.95%

TRISULPHONES.

<page 14.>

Bis(ethylsulphonyl)phenylthiomethane (~~X = Y = Et, Z = Ph~~) was obtained by Fromm's method[4] in 30% yield (m.p. 83°) and from bis(ethylsulphonyl)methane (10 g.), phenyl disulphoxide (12.5 g.), and sodium ethoxide in 65% yield (m.p. 88°). Either sample gave bis(ethylsulphonyl)phenylsulphonylmethane with alkaline permanganate in 80% yield (m.p. 165°); the bromo-derivative prepared by adding the calculated amount of bromine in KBr solution to a cold saturated solution of the trisulphone had m.p. 134° (compare Laves). The use of excess of disulphoxide gave no sign of the disubstitution which Smiles (loc. cit.) found with $CO.CH_2.CO$ compounds, for the reaction product was practically all soluble in aqueous alkali. An attempt to obtain the trisulphone directly from bis(ethylsulphonyl)methane and benzezesulphonyl chloride gave unexpectedly bis(ethylsulphonyl)chloromethane, m.p. 96°.

.1170 g. .1130 g. CO_2 and .0420 g. H_2O

whence C, 26.3 ; H, 4.0.

$C_5H_{11}O_4ClS_2$ requires C, 25.8 ; H, 4.7%.

Methylsulphonylethylsulphonylphenylthiomethane (~~X = Me, Y = Et, Z = Ph~~) was obtained from methylsulphonylethylsulphonylmethane and phenyl disulphoxide, purified by sublimation, and recrystallised from benzene ; m.p. 126°. (Found : C, 40.5 ; H, 5.0)

0.3490 g. neutralised 12.30 c.c. N/10 NaOH

whence equivalent 284

$C_6H_{14}O_4S_3$ requires C, 40.8 ; H, 4.8%. equiv.,294.

Phenylsulphonylethylsulphonylmethylthiomethane, obtained from phenylsulphonylethylsulphonylmethane, methyl p-toluenethiosulphonate, and sodium ethoxide, had m.p. 98° (methyl alcohol)

4.17 mg. gave 6.225 mg. CO_2 and 1.82 mg. H_2O.

whence C, 40.8 ; H, 4.85.

$C_{10}H_{14}O_4S_3$ requires C, 40.8 ; H, 4.8%.

Phenylsulphonylmethylsulphonylethylsulphonylmethane (**I**) was obtained by oxidation of either of the two preceeding compounds. The product from the former melted at 216°, that from the latter at 216 - 219°, and a mixture of the two at the same temperature.

4.335 mg. gave 5.995 mg. CO_2 and 1.88 mg. H_2O.

0.4034 g. neutralised 12.6 c.c. N/10 NaOH.

0.2035 g. " 6.45c.c. " "

0.4078 g. " 12.7 c.c. " "

whence C, 37.3 ; H, 4.7% equivalent 319, 316, 321.

$C_{10}H_{14}O_6S_3$ requires C, 36.9 ; H, 4.3 equiv., 326.

It is sparingly soluble in all the usual cold solvents, but does not separate from pure water until a few drops of mineral acid are added. It is acid to thymol-blue, and as it is not precipitated from its salts by acetic acid, it can thus be conveniently freed from any unoxidised generator. The bromo-derivative has m.p. 141° .

4.66 mg. gave 5.10 mg. CO_2 and 1.42 mg. H_2O.

whence C, 29.8 ; H, 3.4.

$C_{10}H_{13}O_6BrS_3$ requires C, 29.7 ; H, 3.2%.

The brucine salt of the trisulphone was obtained by crystallising the substances in the requisite proportions from a mixture of alcohol (2parts) and chloroform (1 part). It separated in stout prisms, m.p. 140 - 150° (efferv.), and had $[\alpha]_{5461}$ -25.7° (l = 1) in 3.5% aqueous alcohol solution.

0.3141 g. neutralised 4.06 c.c. N/10 NaOH.

(to violet with B.D.H. Universal)

whence equivalent 747.

$C_{35}H_{46}O_{11}N_2S_3$ requires " 766.

The rotation and m.p. were unaltered by repeated recrystallisation, and when the salt was carefully decomposed with ammonia, the ammonium salt was inactive. The cinchonine salt was too soluble to crystallise.

Laevo hydroxy-hydrindamine was obtained exactly as described by Pope and Read[40] by crystallising the racemic base with d-bromo-camphor sulphonic acid (It is very advantageous to recrystallise the bromo-camphor from ligroin before sulphonation).

Dextro hydroxy-hydrindamine (obtained by Pope and Read similarly by use of l-bromo-camphor sulphonic acid) was isolated, without the use of laevo bromo-camphor, by taking advantage of the fact that these active bases are much less soluble than the racemic. Accordingly, the mother liquors from the crystallisation of l-base d-bromo-camphor sulphonate were evaporated, taken up in alcohol and precipitated with hydrochloric acid.

The mixed hydrochloride (rich in dextro) was recrystallised from five times its weight of hot water when about one-half separated being practically pure dextro base hydrochloride.

0.232 g in 20 c.c. water $= +0.39^\circ$ $[\alpha]_D = +34^\circ$

This mother liquor contained a very weakly dextro-rotatory mixture ;

1.4 g. in 10 c.c. water $= 0.5^\circ$ $[\alpha]_D = 3.5^\circ$

This was once more treated with (recovered) d-bromo-camphor sulphonic acid and so a further supply of laevo base isolated.

~~The two active hydroxyhydrindamines were obtained as described by Pope and Read.~~ The trisulphone (2.1 g.) and d-hydroxyhydrindamine (1.0 g.) were refluxed with ethyl acetate (80c.c.) till all had dissolved. On cooling, 85% of the salt crystallised, m.p. 159°.

2.878 mg. gave .076 c.c. N_2 at 20° and 751 mm.

whence N, 2.85

$C_{19}H_{25}O_7NS_3$ requires N, 2.95%.

It is very readily soluble in alcohol, water, and acetone.

Wt in 100 c.c.	Solvent	$[\alpha]_{5461}$
3.3 g.	water	17.3°
7.25g.	dry alcohol	18.5°
6.39g.	acetone	33.2°
		31.7° after 24 hrs.
4.265g.	dry acetone	24.5°
		33.2° after 4 hrs.

When, however, the trisulphone was liberated from the salt , its solutions were inactive. Even by adding the calculated quantity of laevo-hydroxyhydrindamine to a solution containing the salt from the d-base, an inactive solution was obtained, and there was

no sign of any fugitive activity.

Phenylsulphonyl-p-tolylsulphonyl-3:5-dichlorophenylthiomethane, obtained from phenylsulphonyl-p-tolylsulphonylmethane, 3:5:3':5'-tetrachlorodiphenyl disulphoxide, and sodium ethoxide in 90% yield, and recrystallised from alcohol, sintered at 123° and melted at 145°. It was recovered unchanged from attempts to oxidise it with perhydrol or permanganate.

10.19 mg. gave 5.985 mg. AgCl.

whence Cl, 14.6.

$C_{20}H_{16}O_4Cl_2S_3$ requires Cl, 14.6%.

Phenylsulphonyl-p-tolylsulphonylmethylthiomethane, obtained from the same disulphonylmethane, methyl p-toluenethiolsulphonate and sodium carbonate in 60% yield, had m.p. 105°.

4.21 mg. gave 7.83 mg. CO_2 and 1.81 mg. H_2O.

whence C, 50.7 ; H, 4.75.

$C_{15}H_{16}O_4S_3$ requires C, 50.6 ; H, 4.5%.

Phenylsulphonylmethylsulphonyl-p-tolylthiomethane, obtained from phenylsulphonylmethylsulphonylmethane and di-p-tolyl disulphoxide, had m.p. 169°.

.1268 g. gave .2341 g. CO_2 and .0580 g. H_2O.

whence C, 50.3 ; H, 5.1.

$C_{15}H_{16}O_4S_3$ requires C, 50.5 ; H, 4.5%.

Phenylsulphonyl-p-tolylsulphonylmethylsulphonylmethane, II obtained from either of the two preceding compounds by means of perhydrol, melted at 174° , and a mixture at the same temperature.

1.543 mg. gave 2.66 mg. CO_2 and 0.68 mg. H_2O.

whence C, 46.9 ; H, 4.9.

$C_{15}H_{16}O_6S_3$ requires C, 46.4 ; H, 4.1%.

Its salts with cinchonine, brucine, and d-hydroxyhydrindamine showed no tendency to crystallise.

Phenylsulphonylmethylsulphonyl-3:5-dichlorophenylthiomethane, obtained from the disulphonylmethane and the tetrachlorodiphenyl disulphoxide, had m.p. 147°.

.1022 g. gave .1528 g. CO_2 and .028 g. H_2O.

whence C, 40.8 ; H, 3.0.

$C_{14}H_{12}O_4Cl_2S_3$ requires C, 40.8 ; H, 2.9%.

It was oxidised with perhydrol in hot glacial acetic acid for several hours. After removing solvent and excess perhydrol the residue was dissolved in sodium carbonate solution. When acidified with acetic acid, some unchanged thio-methane was precipitated. The trisulphone III was precipitated with hydrochloric acid from the filtrate. Recrystallised from glacial acetic acid. M.P. 208° (becoming blue).

C, 38.4 ; H, 3.3.

$C_{14}H_{12}O_6Cl_2S_3$ requires

C, 38.0 ; H, 2.7%.

No crystalline salts were obtained from this trisulphone.

Ethyl p-toluene thiosulphonate, was originally prepared by Otto[22] as an undistilled oil, by the action of ethyl iodide on the sodium p-toluene thiosulphonate. Ethyl iodide may be advantageously replaced by diethyl sulphate and the oil distilled at 1 mm. at 145 - 150°. The distillate solidified and melted at 32° after recrystallisation from alcohol.

Phenylsulphonyl acetone and ETHYL p-toluene thiosulphonate. Molecular proportions of sodium ethylate and the two above were heated in alcohol. The solvent was removed and the residue warmed with aqueous alkali. The precipitated oil (50 %) was oxidised with permanganate and that portion of the resulting sulphone which dissolved in alkali was recrystallised from hot water. M.P. 109°.

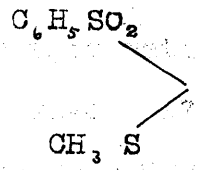
Phenylsulphonylethylsulphonylmethane (page 49) melted at 108 - 110°, but a mixture of the two was quite molten at 100°.

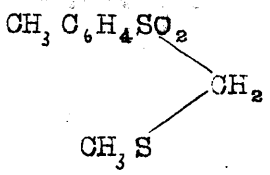
Phenyl sulphonyl acetone and METHYL p-toluene thiosulphonate with sodium ethylate.

After heating the reactants several hours in alcohol, and evaporating off the solvent, the residue was practically all soluble in alkali. On warming that solution an oil was precipitated which soon solidified. Recrystallised from water, m.p. 71°.

4.80 mg. gave 8.72 mg. CO_2 and 2.38 mg. H_2O.

whence C, 49.5 ; H, 5.5

Y (phenyl)  requires C, 47.5 ; H, 4.95.

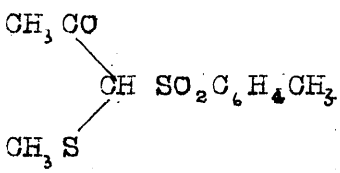
Y(tolyl)  requires C, 50.0 ; H, 5.5%

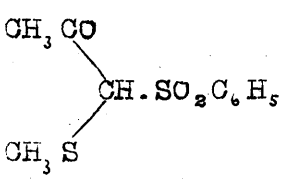
Phenyl sulphonyl acetone and METHYL p-toluene thiosulphonate with sodium carbonate.

The purest materials (30 g., 26 g., and 7 g.) were heated several hours in alcoholic solution and after distilling off alcohol, the residue dissolved in alkali, freed from traces of insoluble matter and precipitated with acetic acid. Yield 16 g. solid. M.P. 65 - 70° Recrystallised from alcohol and then benzene, M.P. 78°.

11.20 mg. gave 20.325 mg. $BaSO_4$

whence S, 24.9.

X (tolyl)  requires S 24.8.

X (Phenyl)  requires S 26.2.

Hydrolysis (to split off acetyl group).

The pure substance was dissolved in the minimum alkali and warmed on water bath until the solution was cloudy. On cooling

11 gms. solidified out and after recrystallisation from alcohol (77°) and twice from water had M.P. 80°.

8.11 mg. gave 17.45 mg. $BaSO_4$. whence S, 29.5.

$CH_3SCH_2SO_2C_6H_4CH_3$ requires S, 29.6.

$CH_3S\ CH_2SO_2C_6H_5$ " S, 31.7.

Oxidation. The sulphide (80°) was oxidised in suspension in very dilute cold sulphuric acid with 2% $KMnO_4$. The MnO_2 was removed by filtration and the filtrate concentrated. The disulphone which separated overnight melted at 139 - 140° after recrystallisation from alcohol.

5.019 mg. gave 7.86 mg. CO_2 and 2.07 mg. H_2O.

4.611 " " 7.245" " " 1.97 " "

10.90 " " 20.72 " $BaSO_4$.

whence C, 42.75, 42.8 ; H, 4.58, 4.75 ; S, 26.1.

Z (tolyl) $CH_3SO_2\ CH_2\ SO_2C_6H_4CH_3$

requires C, 43.6 ; H, 4.85 ; S, 25.8.

P $CH_3SO_2CH_2SO_2C_6H_5$

requires C, 41.0 ; H, 4.2 ; S, 27.4.

Four places where an extra CH_2 group may conceivably be ;

X, The sulphone 139 - 140° could not be methyl sulphonyl phenylsulphonyl ETHANE for that substance melts at 104° and is much less soluble in alkali (page 49) Further, the sulphone '139 - 140°' (2.3 g.) was condensed with 2:5:2':5'-tetrachlorodiphenyl disulphoxide (4 g.) with either sodium carbonate or sodium ethylate and after working up in the usual manner the

resulting dichlorophenylthiol disulphonyl METHANE M.P. 157° is easily soluble in alkali, which a substituted ETHANE surely would not be.

8.88 mg. gave 5.90 mg. AgCl. whence Cl, 16.4.

$CH_3C_6H_4SO_2$

$CH.SC_6H_3Cl_2$ requires Cl, 16.7%.

CH_3SO_2

X_2 The sulphone 139 - 140° could not be ETHYL sulphonyl phenyl sulphonyl methane for that substance melts at 110° (page 49)

X_3 Curiously enough, Phenylsulphonyl METHYL sulphonyl METHANE (page 50) melts practically at the same temperature as the disulphone 139 - 140 but there is no doubt that the mixture melts considerably lower.

X_4 Synthesis of p-TOLYL sulphonyl methylsulphonyl METHANE.

p-tolyl mercaptan (18 g.) was shaken several hours at 100 with formalin (9 c.c.). Methyl mercaptan was added to the ice cooled mixture and a few drops of concentrated hydrochloric acid. After the heat of reaction subsided, any uncombined mercaptans were removed with alkali and the residual oil distilled at 12 mm. The fraction, B.P. 155 - 165° was oxidised with cold dilute permanganate, and after removing the manganese dioxide, the disulphone which separated out, was recrystallised from benzene. M.P. 159°. The disulphone '139 - 140°' was then recrystallised

from benzene twice, rejecting the least soluble fraction. It then melted at 152 - 154° and a mixture with the specimen from p-tolyl mercaptan melted between 154 - 158°.

p-TOLYL sulphonyl acetone (2.1 g.) and methyl TOLYL thiosulphonate (2.0 g.) and sodium carbonate (0.5 g.) heated in alcohol for two hours, then evaporated, extracted with alkali, freed from insoluble, reprecipitated with acetic acid and recrystallised once only from alcohol gave X(tolyl) M.P. 81 - 82°, which did not lower the melting point of the specimen of X(tolyl) described on page ~~60~~ 59.

Hydrolysis with hot dilute sodium carbonate removed the acetyl group and the product after recrystallisation from alcohol melted at 79 - 81° and did not depress the melting point of Y(tolyl) described on page 60.

Oxidation of this product under the same conditions gave a disulphone M.P. 158° which was identical with the disulphone from tolyl mercaptan and also with Z(tolyl) ~~page~~ .

3.36 mg. gave 5.38 mg. CO_2 and 1.53 mg. H_2O.

whence C, 43.8 ; H, 5.05.

$CH_3C_6H_4SO_2$

CH_2 requires C, 43.6 ; H, 4.85.

CH_3SO_2

Methyl benzene thiosulphonate.

Crystallised benzene sulphonyl chloride was gradually added to a 25% solution of sodium sulphide keeping cool till all the sulphonyl chloride had reacted, then shaking for 6 - 7 hours at 40° to dissolve the precipitated sulphur. On concentrating and cooling the sodium benzene thiosulphonate crystallised and was shaken with twice its weight of neutral dimethyl sulphate. The precipitated oil was dried and distilled at 1 mm. The fraction, B.P. 123° was collected.

5.10 mg. gave 8.39 mg. CO_2 and 2.13 mg. H_2O.

4.95 mg. gave 8.18 mg. CO_2 and 2.13 mg. H_2O.

whence C, 44.9, 45.0 ; H, 4.6, 4.8.

$C_6H_5SO_2SCH_3$ requires C, 44.7 ; H, 4.3%.

Phenyl sulphonyl acetone and methyl benzene thiosulphonate.

Equal amounts with sodium carbonate were heated in alcohol solution till the carbonate had dissolved, when the solvent was removed and the portion soluble in alkali precipitated with acetic acid. Recrystallised (alcohol) M.P. 60°.

3.97 mg. gave 7.22 mg. CO_2 and 1.84 mg. H_2O.

whence C, 49.6 ; H, 5.15.

$C_6H_5SO_2\underset{\underset{SCH_3}{|}}{C}HCOCH_3$ requires C, 49.25 ; H, 4.9%.

Hydrolysed with dilute sodium carbonate it gave a sulphide M.P. 84 - 85° (which was not identical with $C_6H_5SO_2CH_3$ M.P. 86° - the hydrolysis product of phenyl sulphonyl acetone).

5.85 mg. gave 10.30 mg. CO_2 and 2.61 mg. H_2O.

whence C, 48.0 ; H, 4.95.

$C_6H_5SO_2CH_2SCH_3$ requires C, 47.5 ; H, 4.95%.

Oxidised with dilute permanganate it gave a disulphone M.P. 145° (from benzene) identical with Phenyl sulphonyl methyl sulphonyl methane 146° (see page 50)

The above three compounds melt at temperatures quite near those of the series X(tolyl), Y(tolyl), Z(tolyl), but in each case mixed melting point determinations shewed marked depression.

Phenyl sulphonyl acetone (5 mols.) and methyl p-toluene thio-sulphonate (1 mol.) with sodium carbonate. The alkali soluble reaction product was precipitated with acetic acid and the resulting solidified oil hydrolysed with sodium carbonate. The sulphide melted at 78 - 81° and was evidently a very pure sample of either:-

$CH_3C_6H_4SO_2CH_2SCH_3$ 80 - 81°.

or $C_6H_5SO_2CH_2SCH_3$ 84°.

for a small amount of either lowers the melting point of the other to 60 - 70°. The sulphide was accordingly crystallised from water, rejecting the very first crop. The main crop melted at 80 - 83° whether alone or mixed with the PHENYL sulphonyl compound.
A mixture with the p-TOLYL compound melted about 63°.

p-Toluene sulphonyl acetone (1 mol.) and methyl Benzene thio-sulphonate (3 mols.) with sodium carbonate gave :-

$C_6H_5SO_2CH.SCH_3$
$\quad\quad|$
$\quad COCH_3$ M.P. 59° alone or

mixed with an authentic specimen. On hydrolysis it gave $C_6H_5SO_2CH_2.SCH_3$ M.P. 78 - 79° unchanged by the PHENYL derivative, but depressed below 70° by the corresponding p-TOLYL.

Ethyl phenyl sulphonyl acetate (1 mol.) and methyl benzene thiosulphonate (1mol.) gave crystals (from alcohol) M.P. 81 - 84°.

5.69 mg. gave 10.07 mg. CO_2 and 2.65 mg. H_2O.

whence C, 48.3 ; H, 5.2.

$C_6H_5SO_2CH.COOC_2H_5$ requires
$\quad\quad|$
$\quad SCH_3$ C, 48.2 ; H, 5.1%.

Hydrolysed with warm sodium carbonate a crystalline precipitate was obtained, melting also at 84°, but quite definitely different (mixed ···· 62° ·····). The precipitate was $C_6H_5SO_2CH_2SCH_3$ (mixed M.P. 84°)

Ethyl phenyl sulphonacetate (1 mol.) and methyl p-toluene thiosulphonate (3 mols.) with sodium carbonate after an hour's reaction gave a product which was evidently a mixture (M.P. about 65°), but after 20 hours reaction the alkali soluble reaction product was hydrolysed and the precipitated solid recrystallised from hot water, M.P. 79° unchanged by $CH_3C_6H_4SO_2CH_2SCH_3$, but very considerably depressed (··· 65°) by admixture with $C_6H_5SO_2CH_2SCH_3$.

4-Chlorophenyl sulphonyl acetone was prepared by refluxing

chloroacetone in alcohol with a slight excess of sodium 4-chloro-benzene sulphinate.[41] The alcohol was evaporated and the product poured into water. Recrystallised from alcohol, it melted at 79°.

4.06 mg. gave 6.95 mg. CO_2 and 1.45 mg. H_2O.

whence C, 46.7 ; H, 3.97.

$Cl.C_6H_4SO_2CH_2COCH_3$ requires C, 46.5 ; H, 3.85%.

Chlorophenyl sulphonyl acetone (0.9 g.) methyl p-toluene thio-sulphonate (4.0 g.) with sodium carbonate gave a reaction product almost all soluble in alkali. The alkaline extract was acidified with acetic acid and the precipitated solid recrystallised from chloroform-ligroin. It was free from halogen and melted at 78° either alone or admixed with $CH_3C_6H_4SO_2\underset{SCH_3}{\overset{|}{C}}HCOCH_3$. The acetic acid filtrate gave a precipitate of impure sulphinic acid M.P. 75 - 85° containing chlorine. (cf. p. 72)

PHENYL sulphonylacetophenone (1 g.) with methyl p-TOLYL thio-sulphonate (5 g.) with sodium carbonate gave after hydrolysis of the alkali soluble reaction product crystals M.P. 80° identical with $CH_3C_6H_4SO_2CH_2SCH_3$.

THIO ARYL EXCHANGE ?.

Phenylsulphonylacetone[42] (1 mol.) and phenyl disulphoxide with sodium ethoxide gave crystals from alcohol M.P. 69 - 70°.

3.64 mg. gave 7.82 mg. CO_2 and 1.86 mg. H_2O.

whence C, 58.6 ; H, 5.7.

$C_6H_5SO_2CH(SC_6H_5).COCH_3$ requires C, 58.8 ; H, 4.6%.

p-toluene sulphonyl acetone (1 mol.) and p-tolyl disulphoxide (1 mol.) (sodium ethoxide) gave crystals from alcohol M.P. 98 - 100° not identical with $C_6H_5SO_2CH(SC_6H_4CH_3).COCH_3$ M.P. 97° (mixed M.P. 78 - 81°).

3.14 mg. gave 7.04 mg. CO_2 and 1.49 mg. H_2O.

whence C, 61.1 ; H, 5.3.

$CH_3C_6H_4SO_2CH(SC_6H_4CH_3).COCH_3$ requires C, 61.1 ; H, 5.4%.

PHENYL sulphonyl acetone (1 mol.) and p-tolyl disulphoxide (5 mols) (sodium ethoxide) gave after two days refluxing in alcohol, crystals M.P. 94° unchanged by admixture with $C_6H_5SO_2CH(SC_6H_4CH_3).COCH_3$ but depressed below 75° by $CH_3C_6H_4SO_2CH(SC_6H_4CH_3)COCH_3$.

p-TOLYL sulphonyl acetone (1 mol.) and PHENYL disulphoxide (5 mol.) gave crystals M.P. 85° (alcohol)

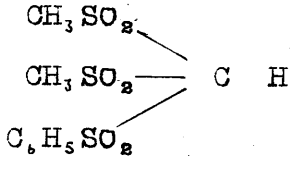
5.19 mg. gave 11.41 mg. CO_2 and 2.44 mg. H_2O.

whence C, 60.0 ; H, 5.2.

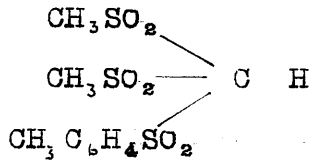
$CH_3C_6H_4SO_2CHCOCH_3$ (with SC_6H_5 on the CH) requires C, 59.8 ; H, 5.0%

DISULPHONYL METHANE EXCHANGE ?

Reference compounds



'Phenyl' trisulphone



'p-tolyl' trisulphone.

'Phenyl' was prepared by heating bismethylsulphonyl methane (1.7 g) with phenyl disulphoxide (2.5 g.) and sodium ethoxide and oxidising the disulphonyl thiomethane with permanganate. Recrystallised from water the 'phenyl' trisulphone melted at 225° .

.1130 g. required 5.2 c.c. 0.0662 N $Ba(OH)_2$

whence equivalent 328 'Phenyl' trisulphone requires 312.

'TOLYL' was prepared by condensing bismethylsulphonyl methane (0.35 g.) with p-tolyl disulphoxide (1.4 g.) with sodium ethoxide.

The resulting disulphonylthiomethane M.P. 137° was oxidised with permanganate and gave a trisulphone M.P. 185° (from water).

3.95 mg. gave 5.29 mg. CO_2 and 1.58 mg. H_2O.

whence C, 36.6 ; H, 4.4.

$(CH_3SO_2)_2$

$\diagdown$

CH requires C, 36.8 ; H, 4.3%.

$\diagup$

$CH_3C_6H_4SO_2$

Possible Exchanges :-

p-TOLYL sulphonyl methyl sulphonyl methane (0.2 g.) with methyl PHENYL thiosulphonate (3.0 g.) with sodium carbonate gave a disulphonyl thiomethane which on oxidation gave a trisulphone M.P. 185° identical with the above 'tolyl' trisulphone M.P. 185°.

PHENYL sulphonyl methyl sulphonyl methane (0.5 g.) and methyl p-TOLYL thiosulphonate (5 g.) gave a disulphonyl thiomethane M.P. 147° which was oxidised to a Trisulphone M.P. 225° identical with the above 'phenyl' trisulphone M.P. 225°.

The reaction between silver benzene sulphinate and bis ethyl sulphonyl dibromomethane.

The dry reactants (7 g. and 11 g.) were refluxed in ether till there was a considerable precipitate of silver bromide. After removal of the ether, dilute acetic acid extracted bis ethyl sulphonyl methane (2 g.) and there was no trace of bis ethyl sulphonyl, phenyl sulphonyl methane (soluble in sodium acetate)

The reaction between phenyl sulphonyl methyl sulphonyl methane (.44 g.) and di-tolyl disulphone (.52 g.).

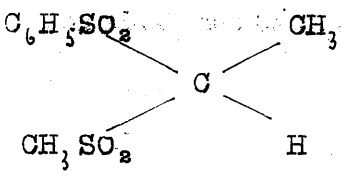
The reactants were heated in alcohol with sodium ethoxide and after all had gone into solution, the solvent was removed and the alkali soluble residue acidified with acetic acid. The precipitate was largely soluble in hot water (unchanged sulphonyl methane) and the insoluble part after recrystallisation from dilute acetic acid melted at 169° whether alone or mixed with $C_6H_5SO_2 \diagdown CH \diagup CH_3SO_2$ $SC_6H_4CH_3$

The filtrate from the acidification with acetic acid gave no further precipitate with hydrochloric acid, indicating the absence of $C_6H_5SO_2 \diagdown CH \diagup CH_3SO_2$ $SO_2C_6H_4CH_3$

Methyl p-Toluene sulphonate (1.9 g.) and phenyl sulphonyl methyl sulphonyl methane (2.4 g.)

The reactants stood overnight in alcohol with sodium ethoxide. After heating for a short time the solvent was evaporated. The residue insoluble in alkali was recrystallised from benzene

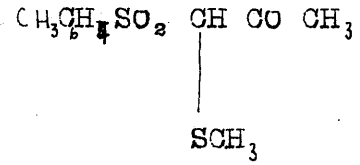
M.P. 101° not depressed by



Yield 0.8 gm.

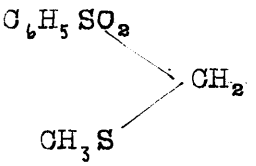
The alkali soluble extract contained a little (0.2 g.) of the unchanged sulphonyl methane.

The reaction between methyl benzene thiosulphonate (4 g.) and

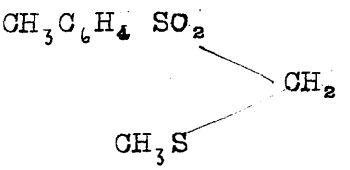


(1 g.) and Na_2CO_3

The reactants were heated in alcohol 4 hours. The solvent was distilled off and the residue extracted with sodium hydroxide. The alkaline extract was acidified with acetic acid and the precipitated oil hydrolysed with sodium carbonate. The crystals which separated, after recrystallisation from ligroin, melted at 80° whether alone or mixed with



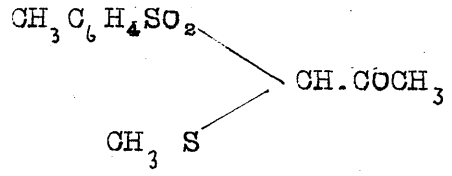
but the mixture with



was liquid below 67°.

On the other hand, in the absence of one molecular proportion of

sodium carbonate no exchange took place, for even after much longer heating the product isolated melted at 79 whether alone or mixed with



Excess 4-chlorophenylsulphonylacetone (5 g.) and methyl p-toluene thiosulphonate (1 g.) in alcohol with sodium carbonate (0.3 g.) gave an alkali soluble product which on hydrolysis gave crystals M.P. 93° from dilute acetic acid. (Cf. p. 66).

4.91 mg. gave 7.26 mg. CO_2 and 1.84 mg. H_2O

whence C 40.4 H 4.2

$ClC_6H_4SO_2-CH_2$ requires
SMe

C 40.6 H 3.8%